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Title Method, apparatus and components of dialysis systems

Field of the Invention

The invention relates to method, apparatus and components of dialysis systems, such as peritoneal dialysis, hemodialysis, hemodiafiltration or hemofiltration systems.

Background of the Invention

Kidney dysfunction is a serious and life-threatening condition wherein the kidneys of a mammal do not function properly to remove impurities, remove excess water and perform other physiologically important activities. A person affected with kidney dysfunction needs to undergo regular dialysis treatments so that the blood can be purified and water removed.

In one type of conventional dialysis procedure, peritoneal dialysis (PD), a PD fluid is administered to the peritoneal cavity of a mammalian patient to dwell there and later be removed as a spent dialysate. Waste products are transferred to the PD fluid and are removed together with the spent dialysate. An osmotic agent in the PD fluid causes removal of excess water. A buffer in the PD fluid causes replenishment of the body buffer. Further electrolytes are balanced by the PD fluid.

Because PD fluid is passed into the patient's body there is a risk of infection, which sometimes results in peritonitis.

For performing peritoneal dialysis, couplings are used for connecting a catheter ending in a peritoneal cavity to a source of PD fluid. In an attempt to reduce patient infection, such couplings are made as "aseptic" or "sterile" couplings. Although aseptic couplings aid in reducing contamination of PD fluid, each coupling may permit entry of potentially harmful microorganisms, such as bacteria and fungi, into an otherwise

sterile PD system, and, eventually, being transfer to the peritoneal cavity. Reducing the number of these couplings may reduce the risk of infection and peritonitis.

Traditionally, sterile PD fluid is stored in, and administered to a patient from, a plastic fluid bag. An aseptic coupling is typically used to connect the fluid bags to the catheter of the patient. Each coupling increases the chances of bacterial and other contamination.

The two most common forms of PD, namely, continuous ambulatory peritoneal dialysis (CAPD) and automatic peritoneal dialysis (APD), require many fluid bags to be used per year. CAPD normally relies on gravity to fill and drain PD fluid originating in a bag set and provides continuous treatment while the patient is still relatively free to move. Fluid exchanges are normally performed during the daytime. APD relies on the use of a cycler for pumping PD fluid from fluid bags to perform patient fill and drain cycles, usually overnight, while the patient is asleep. In both cases, a particular prescription of PD fluid is manufactured and packeaged in one or more bags under sterile conditions at a production plant, and the bags are then shipped to a patient or physician.

However, the use of PD fluid bags has a number of drawbacks and disadvantages. Every patient has different dialysis requirements, and those requirements may be different at different times, and therefore benefits from use of a PD fluid that specifically meets the patient's needs. As a result, manufacturers of PD fluid have to make and deliver many different formulations of PD fluid. This often requires storage of a significant number of bags containing different PD fluid formulations in the home of a patient.

Clinical testing is being performed today using bicarbonate as a buffer instead of conventional lactate buffered PD fluid. Conventional PD fluids have a relatively low pH, which may cause discomfort and even pain during the fill phase. By using bicarbonate as a buffer, PD fluids having a physiological pH may be formulated. However, over time, calcium carbonate, formed from components of the PD fluid, may precipitate out of the solution of the PD fluid, rendering the

solution unusable.

Glucose, another component of PD fluid, may degrade over time particularly when the PD fluid has been subject to conventional heat sterilisation in an autoclave. The degradation of glucose may produce degradation products which are potentially harmful to the patient, at least in the long term.

PD fluid bags are often shipped a significant distance from the point of manufacture to the point of use. Since a large proportion of PD fluid is water, this effectively amounts to transporting large quantities of water from PD fluid production plants to treatment locations, such as hospitals, clinics or patients' homes.

Further, the size of PD fluid bags is limited because they muust be sufficiently lightweight to permit easy handling by a patient or physician. Most PD fluid bags for CAPD contain a relatively small amount of fluid, for example between 0.5 and 5 litres. When higher volumes are required, such as in APD, multiple PD fluid bags may be used during each treatment session. Having more than one PD fluid bag, however, necessitates an aseptic coupling for each bag and requires relatively complicated connection and disconnection procedures when changing bags. These additional connection and disconnection procedures, although aseptic, provide an opportunity for potentially harmful bacteria to enter the dialysis system and cause peritonitis. Four or five connections may be involved in APD.

In dialysis, specifically acute hemodialysis, bags of sterile dialysis solution are used. During hemofiltration and hemodiafiltration, infusion solutions are used for infusion into the blood. Such solutions have the same problems as outlined above.

In U.S. Patent No. 4,718,890, U.S. Patent No. 4,747,822, U.S. Patent No. 5,004,459 and U.S. Patent No. 5,643,201, it has been proposed to make up and administer PD fluid at a treatment location. However, these proposed approaches have various drawbacks and disadvantages. U.S. Patent No. 5,643,201 is illustrative. It discloses a system for preparation of PD

fluid, using a concentrated dialysis liquid source as a starting point. In the system, water is purified in a reverse osmosis unit and is then mixed by a volumetric proportioning pump with the liquid concentrate. Additional dextrose solution may be added by a dextrose pump. The mixed fluid is heated to a temperature of 70°C to 80°C and is then cooled to a proper patient temperature, passed to a reservoir where it is weighed to check the amount, and then delivered to the peritoneal cavity of the patient. Since this system uses a concentrated solution as the PD fluid concentrate, there may be problems due to the stability of the concentrates, for example if bicarbonate buffer is used. In addition, the proposed temperature of 70°C to 80°C may not be adequate to achieve a sufficiently high level of sterilisation.

Further, although there is an option of adding additional dextrose, the relative concentrations of the electrolyte components of the PD fluid are fixed by their relative concentrations in their initially concentrated form. Thus the basic formulation of the PD fluid, apart from the dextrose concentration, is predetermined in advance by the proportions of the constituent substances in the initial concentrated dialysis liquid source. If the system were to be useable with different prescriptions, it would be necessary to provide a range of different concentrated dialysis liquid sources each having the constituent substances present in the appropriate proportions for that prescription. Thus, a range of sources, such as bags of concentrated dialysis liquid, would be required, leading essentially to the same logistic problem as in the PD treatment systems where the PD fluid is entirely pre-prepared at a remote point of manufacture.

Another proposal for making aqueous solutions for medical purposes, including PD fluid, is disclosed in GB 1450030. This also uses a concentrated solution as a starting point. Relative concentrations of electrolyte are predetermined by the starting concentrated solution. This proposal from 1972 does not provide detail on how the PD fluid would be delivered to a patient.

In light of the foregoing, there is a need in the art for improving peritoneal dialysis techniques.

Summary of the Invention

Accordingly, the present invention is directed to apparatus and methodology that substantially obviate one or more of the short-comings or disadvantages of the related art.

One object of the invention is to prepare a medical fluid at a patient treatment site by mixing substantially water with one or more concentrates. The fluid may be prepared with ordinary tap water. As a result, a patient's treatment requirements can be met through a compact package of concentrates, as opposed to multiple bags of fluid. This is convenient both for the patient and for the patient's doctor. It also reduces weight and volume and, accordingly, storage and transportation costs, as well as improving the logistics. Fewer disposable components may be used, involving the use of less plastic, and giving significant environmental advantages.

Another object of the invention is to provide one or more components of medical fluid in at least substantially dry form to increase shelf life and/or problems associated with component precipitation. At least glucose may be provided in substantially dry form.

An additional object of the invention is to provide a universal or near-universal (referred to as "universal" herein) container for filling multiple patient prescriptions. The administering machine is controlled to mix the appropriate prescription at the treatment site. As a result, multiple prescriptions can be obtained using a universal container or cartridge. This reduces the need to inventory multiple prescriptions.

Still another object of the invention is to provide a container containing at least one concentrate in combination with a cleaning agent. In this way, the treatment and cleaning agents are conveniently packaged together.

Yet another object of the invention is to provide a medical treatment apparatus having a reduced number of aseptic connections. There may be zero or only one aseptic connection. This reduces the risk of infections such as peritonitis.

A further object of the invention is to provide a system

whereby a patient's prescription can be electronically communicated to the dialysis machine, such as through a smart card. In this way, if a patient's prescription changes, the machine can be reprogrammed, while continuing to use the same universal cartridge.

A yet further object of the invention is to provide a system offering higher fluid doses in peritoneal dialysis treatment without significant additional cost, unlike in conventional peritoneal dialysis systems in which the cost is roughly proportional to the fluid volume. Higher fluid volumes also may mean that a patient, who would normally be switched from conventional PD to another mode of treatment, such as hemodialysis (HD) because conventional PD provides inadequate treatment, may be kept on PD for a longer time.

A still further object of the invention is to provide a system for sterilising peritoneal dialysis fluid immediately before delivery to a patient to minimise the chance of viable bacteria entering the peritoneum.

It should be understood that the invention could still be practised without performing one or more of the objects and/or advantages set forth above, or by imperfectly performing certain of the objects and/or advantages. Still other objects and advantages will become apparent from the following description of the invention and the claims.

To achieve these and other objects and advantages, and in accordance with the purpose of the invention, as embodied and broadly described herein, the invention includes a number of aspects.

Viewed from a first aspect, the invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:

a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;

a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;

a steriliser arranged to sterilise at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a patient,

characterised in that

at least one of the concentrates is in substantially dry form and, in use of the apparatus, is at least partially dissolved to form part of the peritoneal dialysis fluid.

The invention also provides a method of producing peritoneal dialysis fluid at a treatment location and introducing the fluid into the peritoneal cavity of a patient, the method comprising:

providing a plurality of concentrates of constituents of the peritoneal dialysis fluid in respective chambers;

mixing the concentrates with liquid to obtain peritoneal dialysis fluid;

sterilising at least one of the liquid and the peritoneal dialysis fluid; and

introducing the peritoneal dialysis fluid to the peritoneal cavity of a patient;

characterised in that

at least one of the concentrates is in substantially dry form and is at least partially dissolved to form part of the peritoneal dialysis fluid.

By providing a concentrate in substantially dry or solid form, for example as a powder, the problems associated with liquid concentrates, such as precipitation, short shelf-life etc., can be minimised.

At least one of the concentrates is an osmotic agent, such as a carbohydrate, gluconate, peptides, ketoacid, glycerol, glucose polymer, disaccharide, etc. In one embodiment, the osmotic agent is glucose or dextrose. When glucose is provided as a solution, it generally has a limited shelf-life before it has to be used. By providing the osmotic agent in substantially dry or solid form and then dissolving it at the point of use, its shelf-life may be increased.

At least one of the concentrates is a buffer, such as bicarbonate, lactate, acetate, pyruvate, hydroxybutyrate, phosphate, etc. In one embodiment, sodium bicarbonate or sodium

lacate or a combination thereof, is used as a buffer. By providing sodium bicarbonate in substantially dry or solid form, problems with solutions degrading by the precipitation of solids can be avoided. Sodium bicarbonate is sometimes favoured as a buffer for physiological reasons, but often another buffer is used in peritoneal dialysis. Thus, the use of substantially dry sodium bicarbonate, which is then freshly dissolved into solution at a treatment location, in a peritoneal dialysis treatment system is beneficial.

A concentrate provided in a particular chamber may comprise more than one substance, for example some or all of the electrolytes may be provided in one chamber, and an osmotic agent may be provided in another chamber. In one embodiment, each concentrate comprises a separate constituent substance of the peritoneal dialysis fluid. For the production of a peritoneal dialysis fluid, each chamber may contain a separate constituent substance of the peritoneal dialysis fluid, selected from a group comprising: sodium chloride, sodium bicarbonate, magnesium chloride, calcium chloride, sodium lactate, lactic acid and glucose.

One or more of the concentrates may be provided in liquid form, and one or more of the concentrates may be provided in substantially dry form. In one embodiment the concentrates comprise: sodium chloride in substantially dry form; sodium bicarbonate in substantially dry form; magnesium chloride in substantially dry form; calcium chloride in substantially dry form; lactic acid solution; and glucose in substantially dry form.

By providing a plurality of concentrates of the constituents of peritoneal dialysis fluid in respective chambers, in accordance with the first aspect of the invention, it becomes possible to produce peritoneal dialysis fluids of different formulations. The apparatus comprises a controller for controlling the fluid mixer to produce such different formulations. There is thus provided a choice of formulations which can be made using the plurality of concentrates and liquid, such as purified water. For example, a single disposable container containing the concentrates can be used to

produce different formulations as required by a prescription of a patient. This is considerably more convenient than the currently available systems for providing peritoneal dialysis fluids to a patient, in which the manufacturer stocks a range of bags of fluids of different formulations and the user has to be supplied with and choose the right bag for his or her treatment. Instead, the user can always be supplied with the same plurality of concentrates, which can then be used by the apparatus to make the required formulation.

In one embodiment, the concentrates comprise a plurality of electrolytes and the controller is operable to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes. Thus, rather than being able merely to vary the concentration of osmotic agent (e.g. glucose), the apparatus can vary the relative concentrations of the electrolytes in the peritoneal dialysis fluid according to a patient's prescription. This is an advance over the previously proposed systems for producing peritoneal dialysis fluid at a treatment location using a single combined source of electrolytes. The electrolytes used in the peritoneal dialysis fluid may be one or more of sodium bicarbonate, sodium chloride, sodium lactate, magnesium chloride and calcium chloride.

The controller is in one embodiment provided with data input means for receiving prescription information for a patient. Such data input means may comprise a keyboard or touch screen or the like for a person to input the required prescription information. In one embodiment, the data input means comprises a memory device, for example a smart card, which may be inserted in a suitable part of the apparatus. Alternatively, or additionally, the data input means may comprise a modem or other means enabling remote communication, for example for supervision or for transmission of prescription information to the apparatus.

It is possible to effect dissolution of substantially dry or solid concentrates in the chamber in which it is supplied. In the case of some concentrates, a relatively large quantity of solution may be needed, such that the chamber will generally

not be large enough, without becoming cumbersome, to receive enough water to dissolve all the concentrate. Examples of such concentrates in a peritoneal dialysis solution are sodium chloride and sodium bicarbonate. In these cases, more than a single chamber volume of water is used to dissolve the concentrate. One way of doing this would be to fill the chamber with water via an opening, then to empty the chamber by a reversed flow through the same opening, using an air vent to allow air in to fill the chamber during emptying (if the chamber walls are relatively rigid, an air vent not being necessary in the case of a flexible walled chamber). Filling would then take place again and the process would be repeated as many times as necessary.

In another arrangement, the apparatus is arranged to prime said at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is only partially dissolved when the chamber is filled with liquid, the apparatus further comprising a flow line for removing liquid comprising dissolved concentrate from the chamber, and a flow line for substantially simultaneously adding the same amount of liquid as removed to said chamber.

With such an arrangement, after initial priming a continuous flow to the fluid mixer can be obtained, rather than a periodic flow, reducing the number of cycles required, and thus the opportunities for inaccuracies, for a given batch of peritoneal dialysis flluid. Thus, two flow lines are provided for simultaneous use. One of these may conveniently be used for priming, and the other for venting air from the container, an air vent being necessary in the case of a rigid walled chamber. The concentrate removal flow line may be used during priming to introduce the liquid comprising water to the chamber, and the liquid adding flow line is used during priming to vent air from the chamber. During normal use, venting is not required.

Such a first type of chamber or partial dissolution chamber is suitable for containing sodium chloride or sodium bicarbonate for making the peritoneal dialysis fluid.

A second type of chamber is contemplated for other constituents of the peritoneal dialysis fluid, such as calcium chloride and magnesium chloride. In the case of these concentrates, they are generally only required in relatively small quantities and at low concentrations in the peritoneal dialysis fluid, and so a relatively small chamber can have an adequate volume such that one liquid fill will result in a sufficient amount of dissolved concentrate. Therefore, the apparatus may be arranged to prime said at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is fully dissolved when the chamber is filled with liquid. With this type of chamber, the priming inflow can conveniently use the same flow line as that used to remove dissolved concentrate from the chamber. In the case of a rigid walled chamber, an air vent may be provided to vent air during priming and emptying.

A third type of chamber may be used for the osmotic agent, normally glucose. It is provided in substantially dry or solid e.g. powder form, and the apparatus will then be suitably equipped to stir, agitate or recirculate the glucose once liquid comprising water has been added. This is because of the relative difficulty in achieving rapid dissolution of glucose. In one embodiment of the apparatus, a respective chamber contains an osmotic agent, e.g. glucose, and the apparatus comprises a flow circuit for introducing liquid comprising water into the osmotic agent chamber, for removing liquid comprising dissolved osmotic agent from the chamber and for re-introducing the liquid comprising dissolved osmotic agent into the chamber. Dissolution e.g. of glucose is generally promoted by heating the diluent liquid, for example to 40°C. Heated liquid may initially be supplied to the glucose chamber. It is desirable to maintain the glucose heated during dissolution and circulation, and advantageously therefore a heater is provided for heating the liquid comprising dissolved glucose as it circulates round the flow circuit.

Since glucose powder tends to release gas bubbles during

dissolution, the apparatus may have a vent to allow escape of gas as the liquid comprising dissolved glucose circulates round the flow circuit.

The plurality of chambers containing respective concentrates may be provided by more than one container. It is, however, convenient for a user if all the ingredients for making the peritoneal dialysis fluid are provided in a single container. In one embodiment, the plurality of chambers are defined by a disposable container. In another embodiment, each chamber is in the form of a compartment of a container.

It will thus be appreciated that a plurality of different types of chamber may be provided to deal with the different requirements of the different constituents of the peritoneal dialysis fluid, i.e. taking account of the amount of each constituent normally required and the ease or difficulty in dissolving each constituent. From the user's perspective, however, there is the benefit that all the chambers and the constituents of the peritoneal dialysis fluid which they contain can be provided in a single container. This can provide all constituents needed for an overnight peritoneal dialysis treatment session, which may for example involve the use of 8-30 litres of peritoneal dialysis fluid or more, without the user having to set up the several bags of fluid which would be required with conventional peritoneal dialysis treatment.

It is possible to support the container on the apparatus in a fixed position and then for the apparatus to have a chamber communicating portion, e.g. a spike, which moves to a position communicating with the interior of a said chamber. In one embodiment, the apparatus comprises a container engaging portion for engaging the container and urging the container to a position in which the chambers are opened for communication with respective portions of the apparatus.

In general, it will be desireable to place the container in a location where it can be engaged by the container engaging portion. One way of doing this is for a user to slide the container to the engagement location in a first direction, for example in a horizontal direction, and then for the container engaging portion to urge the container to the communicating

position in a second direction, for example in a vertical direction.

The container engaging portion may for example engage a region of the container remote from the region of the chambers where they are to be opened. This may be the base of the container, inverted so that its opening region faces downwardly. In one embodiment, the container engaging portion is arranged to engage a plurality of flanges each provided adjacent to a respective opening of a respective chamber. By effecting engagement adjacent to the openings, reliable urging in the opening region of the container may be achieved. The flanges are for example formed on the necks defining the openings of the respective chambers.

In one embodiment, a flange associated with each opening is engaged, to ensure reliably and positively that each opening is communicated with the chamber communicating portions of the apparatus. It will be appreciated that it is important that all intended communicating paths should be created at the interface between the apparatus and the container. In one exemplary container, there are eight chamber openings where communication is to be effected. One embodiment of the arrangement for achieving the desired reliable interface involves that at least two of the container openings being linearly aligned with each other, and the container engaging portion comprising a pair of laterally spaced members arranged to engage flanges defined on opposite sides of the openings.

In one embodiment of the apparatus, a plurality of spikes are provided for penetrating respective seals of the chambers to open said chambers. Each spike advantageously comprises two fluid flow channels, to allow simultaneous inflow and outflow of liquid or gas to or from the chamber. As will be apparent from the description below, in the case of a chamber containing glucose it is useful to provide three flow channels, whereas for other concentrates two channels are provided. Rather than having to provide a three flow channel spike, there is provided a pair of spikes for penetrating an osmotic agent, e.g. glucose, containing chamber. This can provide three flow channels, two contributed by one spike and the third by the

other spike. In addition, since the osmotic agent chamber will usually be substantially larger than the other chambers, there will be sufficient space on the osmotic agent chamber wall for the provision of two openings.

After the container has been used to supply the ingredients for one or more peritoneal dialysis patient fills, it will be removed and on the next treatment occasion a fresh container will be used. It is beneficial to disinfect the spikes between treatments. The apparatus comprises a cover for covering a said spike when the container is removed to enable the spike to be disinfected. The container engaging portion may be arranged to engage the cover to urge it to its covering position. Thus, the container engaging portion can fulfil both the function of urging the container to its communicating position, and that of urging the cover to its covering position when no container is present.

It will be appreciated that the container described herein itself embodies a number of inventive aspects. A second aspect of the invention is therefore concerned with a container, such as a disposable container.

In one form of the second aspect, the invention provides a container containing in concentrated form all the concentrates, which, when mixed with water, provide sufficient peritoneal dialysis fluid for a full peritoneal dialysis treatment session.

In another form of the second aspect, the invention provides a container containing concentrated components of dialysis fluid, the container comprising a chamber containing powdered glucose and at least one other distinct chamber containing at least one powdered inorganic salt.

In another form of the second aspect, the invention provides a container containing concentrated components of dialysis fluid, the container comprising at least one chamber containing a cleaning agent and at least one other distinct chamber containing at least one powdered inorganic salt. It is advantageous to provide a cleaning agent in the same container as at least one concentrate for making peritoneal dialysis fluid, as this facilitates operation of the apparatus, because

the user is only required to insert one container into the apparatus to provide the concentrated PD fluid and to provide the cleaning agent, rather than separate containers which may be mistaken.

In another form of the second aspect, the invention provides a container containing concentrated components of dialysis fluid, the container having defined therein at least two distinct chambers, each of said chambers containing a different inorganic salt, wherein the volume of each of said chambers and the amount of salt contained within each chamber is such that when a solution of each salt is prepared by filling each of said chambers with liquid, such as water, the conductivities of the solutions so prepared are characteristically different. As described in more detail below, such an arrangement enables the apparatus with which the container is to be used to check that it is receiving the correct concentrate or inorganic salt from each chamber.

In another form of the second aspect, the invention provides a container containing concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein each said connector comprises at least two separate fluid channels, permitting simultaneous inflow to and outflow from the respective chamber. This arrangement allows gas to exit the chamber via one fluid channel as liquid enters via the other fluid channel, and/or it allows gas to enter the chamber via one fluid channel as liquid exits via the other fluid channel, and/or it allows replacement liquid to enter the chamber as liquid exits the chamber. Such an arrangement is particularly useful in the case of chambers having relatively rigid rather than flexible (i.e. collapsible) walls, where the volume of the chamber remains substantially constant whether it is empty or full. By providing the at least two fluid channels as part of the connector, as distinct from providing a vent elsewhere on the chamber, the two fluid channels can be opened up and established only at the time when the container is to be used, such as simultaneously, for example by breaking a seal which

may be in the form of a membrane or septum.

In one arrangement, the at least two fluid channels are arranged concentrically in each of said connectors. This type of connector can for example conveniently mate with a spike which itself has two fluid channels, as described above.

In the case of an osmotic agent, e.g. glucose, containing chamber, it is useful to have more than two fluid channels, notably three. In one embodiment, at least one of said chambers comprises two connectors, one such connector comprising said at least two separate flow channels, and the other connector comprising a further fluid channel.

Again in the case of an osmotic agent, e.g. glucose, dissolution thereof can be advantageously promoted by providing one of the fluid channels with a diffuser to diffuse an inflow of liquid into the chamber.

In one embodiment, the connectors are provided, during operation, in a lower region of the chambers, and one of the fluid channels of at least one connector has a portion extending to an upper region of the chamber. The portion in the upper region can, for example, be used as an air vent, as an inlet for replacement liquid, or for recirculation.

As explained above, at least some of the openings to the chambers are in alignment with each other. There openings mutually aligned along the linear axis. Thus, the connectors can all be engaged by a container engaging portion of the apparatus. The connectors may comprise neck portions each formed with an external flange for engagement by the container engaging portion. A pair of flanges may be provided on opposite sides of the neck portion, or a single flange may extend circumferentially round the neck portion. The container engaging portion may then be in the form of a pair of laterally spaced members - a fork - for engagement with the flanges.

The container should be mountable on or insertable into the machine in a unique manner, to ensure that the correct connectors align with the required communicating portions of the apparatus. In one embodiment, the linear axis of the mutually aligned connectors is offset from a central axis of the container. The container can then interface with the

apparatus in the correct manner only.

In another form of the second aspect of the invention, there is provided a container for use in priming powdered glucose at a patient treatment location, comprising an inlet port in a lower region of the container for receiving a supply of water to dissolve the powdered glucose in the container, wherein said inlet port is provided with a diffuser which is arranged to diffuse the flow of water into the powdered glucose.

In another form of the second aspect of the invention, there is provided a container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein at least two of said connectors are mutually aligned along a linear axis.

In another form of the second aspect of the invention, there is provided a container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising a container body and at least one connector associated with each chamber, wherein there is at least one axis about which the container body is substantially rotationally symmetric, and wherein the connectors are arranged relative to said container body such that the arrangement of connectors is rotationally asymmetric about said axis.

In the manufacture of the container, each chamber may be charged with the appropriate concentrate. It may be problematic successively to charge each chamber of a single container. Therefore, the container may be made as a plurality of sub-containers which are later connected together.

In another form of the second aspect of the invention, the invention provides a method of manufacturing a container for concentrated components of dialysis fluid, the method comprising the steps of:

manufacturing a plurality of individual sub-containers; and

connecting said sub-containers to form said container.

The invention also extends to a container made by the above method.

The apparatus may be connected to a source of purified water, for example a reverse-osmosis unit. In one embodiment, the apparatus comprises a water purifier. The water purifier may, for example, comprise one or more reverse osmosis membrane units. In one embodiment, the water purifier comprises a first reverse osmosis membrane unit, and a second reverse osmosis membrane unit. Each membrane unit has an inlet, a purified water outlet and a waste water outlet. In one embodiment, the purified water outlet of the first membrane unit is in fluid communication with the inlet of the second membrane unit. Moreover, the waste water outlet of the second membrane unit may be in fluid communication with the inlet of the first membrane unit.

According to this arrangement, the water from the waste water outlet of the second RO membrane unit, which is already reasonably pure because it has been through the first RO membrane unit, is recycled and passes through the first RO membrane unit again, so that the overall water consumption of the apparatus is reduced. In this way, two RO membrane units can be used, in order to give a higher purity of water, without increasing the overall water consumption of the apparatus.

The water purifier may comprise, for example upstream of the inlet of the RO membrane unit a coarse filter (for example a 30 micron filter), a fine filter (for example a 5 micron filter), a charcoal filter and/or a water softener. Each of these components prevents blocking of the reverse osmosis membranes.

The water purifier may further comprise a degassing arrangement upstream of the first (or second) RO membrane unit. The water is degassed before it passes through the RO membranes, as a reduction in the amount of dissolved carbon dioxide and other gases in the water can improve the performance of the RO membrane(s). Furthermore, gas bubbles in the water can interfere with the correct operation of the pumps and the like. In general, it is desirable for the water to be degassed at an early stage in the production of the peritoneal

dialysis fluid, as this simplifies the further processing steps, because the dissolved gas content of the water is fixed.

In one embodiment, the steriliser is a heat steriliser.

Viewed from a third aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location comprising:

a water inlet for receiving a supply of water from a mains water supply;

a water purifier for purifying the supply of water from the water inlet;

a fluid mixer for mixing dialysis fluid concentrate with the purified water supply to produce a supply of peritoneal dialysis fluid;

a steriliser for sterilising the supply of peritoneal dialysis fluid; and

a fluid outlet arranged to communicate the sterilised supply of peritoneal dialysis fluid to the peritoneal cavity of a patient,

characterised in that

the steriliser is a heat steriliser arranged for heat sterilisation of the peritoneal dialysis fluid at a sterilising temperature and at an elevated pressure.

Heat sterilisation is generally considered to be effective and safer than, for example, bacterial filtering.

In one embodiment, the steriliser is provided downstream of the fluid mixer so that any bacteria introduced into the peritoneal dialysis fluid during mixing are neutralised. In this way, the production costs of the container for the concentrated components can be reduced, because the components need not be pre-sterilised.

Although the steriliser may be configured to sterilise the peritoneal dialysis fluid itself, alternatively one or more sterilisers may be provided for sterilising one or more of the components of the peritoneal dialysis fluid, such as the liquid, for example water, used to form the peritoneal dialysis fluid and/or the concentrated solutions. If the concentrates are provided as sterile concentrates, only the water used to form the peritoneal dialysis fluid is sterilised.

The steriliser may comprise a sterilisation flow passage and is arranged to heat sterilise the peritoneal dialysis fluid as it flows along the sterilisation flow passage, so that the flow of peritoneal dialysis fluid does not need to be stopped for heat sterilisation. In one embodiment, the apparatus comprises a flow path downstream of the heat steriliser for the flow of sterilised peritoneal dialysis fluid to the patient fill connection, and cooling means for cooling the sterilised peritoneal dialysis fluid as it flows along the flow path, in order that the peritoneal dialysis fluid may be brought to body temperature when it reaches the patient fill connection. The apparatus may be arranged to heat sterilise the flow path prior to its use for the flow of sterilised peritoneal dialysis fluid to the patient fill connection, to ensure that the sterilised fluid travels along a sterilised path.

A fourth aspect of the invention is concerned with systems for dissolving a substantially dry concentrate and delivering the dissolved concentrate to a mixing vessel.

Viewed from a fourth aspect therefore the invention provides apparatus for the production of an aqueous solution for medical use from a plurality of concentrates, the apparatus being arranged to communicate with a plurality of chambers each containing a respective concentrate, at least one of the concentrates being in substantially dry form, the apparatus comprising:

at least one flow line arranged to prime said at least one concentrate in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

a mixing vessel arranged to receive the at least one dissolved concentrate;

a flow regulator associated with the at least one dissolved concentrate arranged to pass the concentrate to the mixing vessel;

characterised by

measuring means arranged to measure a concentration of the at least one dissolved concentrate; and

a pump arranged to pump a metered volume of the at least one dissolved concentrate via the associated flow regulator to

said mixing vessel, whilst measuring by said measuring means the concentration of the dissolved concentrate, so as to deliver a predetermined amount of said dissolved concentrate to said mixing vessel.

The invention also provides a method or providing an aqueous solution for medical use from a plurality of concentrates, comprising:

providing a plurality of concentrates in separate chambers, at least one of the concentrates being in substantially dry form;

priming said at least one concentrate in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

passing the at least one dissolved concentrate to a mixing vessel via a flow regulator associated with that concentrate;

characterised by

adjusting the flow regulator associated with the at least one dissolved concentrate for passing a metered volume of said concentrate through said flow regulator;

measuring a concentration of said concentrate to determine an amount of said concentrate delivered to said mixing vessel; and

terminating said delivering of concentrate when a predetermined amount has been delivered.

Thus, from a starting point of concentrates at least one of which is in substantially dry, e.g. powder, form, an aqueous solution may be obtained in a mixing vessel comprising a predetermined amount of each concentrate, and hence having each concentrate present in a predetermined concentration ratio. Such solution can be prepared to a precise desired formulation, and may be put to medical use, for example for the purposes of peritoneal dialysis, hemodialysis, hemofiltration or hemodiafiltration.

In general, it is intended to obtain a flow of concentrate at a predetermined concentration and this may take time to develop, for example because time is required to achieve dissolution or because adjustments are made e.g. dilution to achieve a flow at the predetermined concentration. It is

beneficial to use the flow as soon as it is established at the desired concentration, rather than to send it to drain whilst awaiting a similar establishment for another concentrate. By providing a mixing vessel in which a known amount of concentrate is to be stored, that concentrate can be passed to the mixing vessel without delay and thus without significant loss to drain.

Where a plurality of concentrates are provided in substantially dry form, each such concentrate is primed to form a dissolved concentrate, a metered volume of each dissolved concentrate is pumped via its associated valve to the mixing vessel, whilst measuring the concentration of the dissolved concentrate, so as to deliver a predetermined amount of the dissolved concentrate to the mixing vessel. Thus, an aqueous solution is obtained comprising a predetermined amount of each concentrate.

Where one or more concentrates are initially provided in liquid form, they may be provided at a known concentration in which case the concentration measuring step may not be necessary, it being sufficient to pump a metered volume to the mixing vessel. However, to be sure of obtaining the right amount of all concentrates in the mixing vessel, it is possible to measure the concentration of such initially liquid concentrates as they are passed to the mixing vessel. This would also be useful where a concentrate is provided initially in liquid form at a concentration which is only approximate. An example of a concentrate which may be provided in liquid form to make e.g. peritoneal dialysis fluid is lactic acid.

Another method therefore comprises adjusting a first flow regulator associated with a first concentrate for passing the first concentrate through the first flow regulator at a metered rate, measuring a concentration of the first concentrate to determine an amount of said concentrate delivered to said mixing vessel, terminating said delivering of said first concentrate when a predetermined amount has been delivered, adjusting a second flow regulator associated with a second concentrate for passing the second concentrate through the second flow regulator at a metered rate, measuring a

concentration of the second concentrate to determine an amount of said concentrate delivered to said mixing vessel, terminating said delivering of said second concentrate when a predetermined amount has been delivered, and repeating said adjusting, passing, measuring and terminating for each further concentrate, thereby to provide an aqueous solution comprising a predetermined amount of each concentrate. Such a method is applicable to a plurality of concentrates in which at least one is provided in substantially dry form, i.e. there may initially be plural, one or no concentrates provided in liquid form. To make dialysis fluid, for example, the electrolytes and osmotic agent may be provided as solid concentrates, e.g. powders, whilst an acid may be provided as a liquid concentrate.

In one embodiment, the apparatus comprises a flow regulator associated with each concentrate, wherein in use of the apparatus a metered volume of each concentrate is pumped via its associated valve to the mixing vessel, whilst measuring the concentration of the concentrate, so as to deliver a predetermined amount of the concentrate to the mixing vessel. For example, there may be a first flow regulator associated with a first concentrate, a second flow regulator associated with a second concentrate, and a further flow regulator associated with each further concentrate.

The pumping of concentrate flows may be effected by a plurality of devices, such as metering pumps, for example one associated with each concentrate. In one embodiment, the pump is arranged for pumping, in turn, each concentrate to the mixing vessel. Thus the use of a pump associated with each concentrate can be avoided, thereby reducing the cost, size and weight of the system, particularly where several concentrates are involved, as will be the case for dialysis liquids, for example.

Similarly, although a plurality of concentration measuring means may be provided, again one associated with each concentrate, each concentrate may alternatively be passed via the same measuring means. This may reduce the cost, size and weight of the system. In addition, because the measuring means measures the concentration of each concentrate individually, it

can be selected or set up to give accurate measurements over a range wide enough to cover the expected individual concentrations. This is intended in a system in which a measuring means is used to measure e.g. the conductivity of the solution accumulating in the mixing vessel, since the conductivity will increase as additional concentrates are added and the measuring means would then be required to be accurate over a wide range, i.e. a range sufficient to cover the conductivity of a first concentrate, the higher conductivity of a first and second concentrate combined, etc. Furthermore, in such a cumulative system, measurement errors resulting from the measurement of the first concentrate will add to the errors in the measurement of the second concentrate and so on, so that later concentrates are measured at a lower accuracy than initial ones. This does not occur when the concentration of each concentrate is measured individually as the errors are due only to the measurement being taken.

The measuring means may comprise more than one measuring device, such as two measuring devices, to provide the system with redundancy and thus additional safety. The measuring means may comprise a pH meter or other type of meter, such as an ion selective meter, but preferably comprises a conductivity meter.

The apparatus may be arranged to dilute a concentrate after it leaves its respective chamber and before it is passed to the mixing vessel. By controlling the amount of dilution, the concentration of the constituent substance delivered to the mixing vessel can be controlled to a predetermined concentration, even starting from different pre-dilution concentrations, which may often be the situation in the case of a concentrate initially provided in substantially dry form. The dilution may for example be effected by a proportioning pump. In one dilution arrangement, it comprises a concentrate flow line along which concentrate is pumped by the pump at a metered rate, a water flow line along which water is pumped by a second pump at a metered rate, the concentrate flow line joining the water flow line so that in use the concentrate and water are mixed to dilute the concentrate before it is passed to the mixing vessel. The concentration of the concentrate or diluted

concentrate is measured, and the pumps are controlled to provide a dilution ratio required in order to obtain a desired concentration of the diluted concentrate.

A convenient method of achieving the delivery of a predetermined amount of concentrate to the mixing vessel comprises passing said diluted concentrate to the mixing vessel at a flow rate, measuring the concentration of the diluted concentrate, multiplying said measured concentration with said flow rate, integrating the product of said multiplication over time to obtain a total amount of concentrate material delivered to said mixing vessel, and terminating said passing of diluted concentrate to said mixing vessel when a predetermined amount of concentrate material has been delivered to said mixing vessel. The apparatus may therefore include a suitable processor for carrying out the multiplying, integrating and terminating functions.

The plurality of chambers containing concentrates will normally be provided in predetermined positions relative to each other and relative to the apparatus to ensure that each concentrate is supplied to the appropriate portion of the apparatus. In one embodiment, the apparatus is able to check that it has received the correct concentrate at each appropriate portion. Therefore, the method comprises measuring a property of a said concentrate or a property of the concentrate after dilution thereof downstream of its respective chamber, and determining from that measurement if the concentrate is the concentrate expected from that chamber.

Whilst the measured property may be pH, for example, it may be difficult to distinguish between concentrates which have a neutral pH at any concentration. In one embodiment, the measured property is conductivity. The concentrates may be provided in amounts in their respective chambers such that when their properties e.g. conductivities are later measured they are distinguishable from each other. The property may be measured in its form as supplied from the chamber, i.e. without further dilution. If it is measured after dilution, then providing dilution is effected by the addition of a known amount of liquid comprising water, then the measurement for the

expected concentrate can still be known.

The concentration of the concentrates in the mixing vessel may provide the final formulation for the required medical use. However, in order that the mixing vessel can be kept to a reasonable size, in one embodiment, the liquid in the mixing vessel is passed towards a point of use and to dilute the liquid downstream of the mixing vessel.

Dilution can be effected by feeding liquid from the mixing vessel into a water conducting line, the mixing vessel liquid being pumped at a known rate and the diluted liquid being pumped at a higher known rate, whereby water is drawn from a source at a flow rate being the difference between the known flow rate of the mixing vessel liquid rate and the known flow rate of the diluted liquid. Thus, the extent of dilution will be known. In order to be sure to obtaining the correct formulation for the diluted liquid, having regard to its medical use e.g. as peritoneal dialysis fluid, it is also checked that the extent of dilution is correct. This may be achieved by providing a suitable measuring means, such as conductivity measuring means. The cost, size and weight of the apparatus may be minimised by measuring the concentration of the concentrates in the diluted liquid downstream of the mixing vessel using the same measuring means as is used to measure the concentration of the concentrates during delivery to the mixing vessel.

Where a common flow path is used at some point downstream of the valve associated with each concentrate, it may be desirable to flush that path (or part thereof) after delivery of one concentrate and before delivery of the next. In one arrangement, the pump is reversible and connectable to a source of liquid, such that in use of the apparatus, after termination of delivery of a said concentrate, the pump is reversed to pump said liquid from the source thereof through the associated flow regulator so as to flush the path between the liquid source and the flow regulator, such as a valve. The liquid used for flushing is preferably water.

It will be appreciated from the foregoing that the system for producing different medical formulations at a treatment

location involves a further inventive aspect. A fifth aspect of the invention is therefore concerned with such a system.

In one form of the fifth aspect, the invention provides apparatus for use at a treatment location which uses a plurality of concentrates and is able to produce from those concentrates a range of different peritoneal dialysis fluid formulations, each such formulation being based on predetermined prescription information and comprising at least one of the concentrates in diluted form.

Such an apparatus is an advance over the known systems for peritoneal dialysis involving the use of a range of pre-prepared formulations, which are made remotely from the treatment location and must then be selected according to the required formulation and transported to the treatment location. Rather, the plurality of concentrates is used by the apparatus to make up the required formulation on site, according to prescription information determined by a physician or other qualified medical professional. This simplifies inventory control for the manufacturer, who no longer has to produce a range of different pre-prepared formulations, but instead can supply the plurality of concentrates. This is also more convenient for the physician and the patient, who no longer need to concern themselves with ensuring that they are supplied with the right pre-prepared bags of fluid.

In another form of the fifth aspect, the invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:

a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;

a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;

a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;

a steriliser arranged to sterilise at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a

patient,

characterised in that

the controller has data input means for receiving predetermined prescription information for a patient and in that the controller is operable to control the fluid mixer to produce a peritoneal dialysis fluid formulation based on the received predetermined prescription information.

Thus, the plurality of concentrates can be used to make the formulation required by a patient and based on a prescription determined in advance of treatment. There is no need to use a different set of concentrates for each formulation, and accordingly no need to have a required set of concentrates delivered to the treatment location. The prescribing process is separated from the delivery process, giving medical practitioners greater freedom to vary a prescription e.g. from one treatment to the next. Because of the greater flexibility in prescribing which is provided, it may be possible to keep some patients on peritoneal dialysis treatment for longer before they have to be switched to hemodialysis treatments.

In one embodiment, the chambers are in the form of compartments of a container and all the concentrates required to make a said peritoneal dialysis formulation are provided in said compartments. Thus a single container of concentrates can be used to make a range of different formulations, again simplifying use of the system for medical practioners and for patients.

The concentrates may comprise a plurality of electrolytes and the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative electrolyte concentrations from each other. Thus, a medical practitioner can vary the relative electrolyte concentrations to take account of a patient's surplus or shortage of certain salts or ions. Again, this can be done without concern for what pre-prepared bag or bags of formulations are available for use at the treatment location.

In a further form of the fifth aspect, the invention provides apparatus for the production of peritoneal dialysis

fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:

a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;

a fluid mixer arranged to mix the concentrates with liquid to produce the peritoneal dialysis fluid;

a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;

a steriliser arranged to sterilise at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal dialysis of a patient;

characterised in that

the concentrates comprise a plurality of electrolytes, and in that the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes.

The advantages of such apparatus will be apparent from the discussions above and below.

It is to be understood that both the foregoing general description and the following detailed description are exemplary and are intended to provide further explanation of, without limiting the scope of, the invention as claimed.

Brief description of the drawings

An embodiment of the invention will now be described by way of example only and with reference to the accompanying drawings, which are incorporated in and constitute a part of the specification. In the drawings:

Figure 1 is a partially schematic perspective view of an apparatus for the preparation of peritoneal dialysis fluid according to an embodiment of the invention;

Figure 1a is a block diagram of a processor system in the apparatus of figure 1;

Figure 2 is a schematic view of a fluid path in the apparatus of Figure 1 in terms of interconnected functional

modules;

Figure 3 is a detailed schematic view of a water preparation module of Figure 2;

Figure 4 is a detailed schematic view of a thermal control and sterilisation module of Figure 2;

Figure 4a is a detailed schematic view of the thermal control and sterilisation module of Figure 4 in an alternative arrangement;

Figure 5 is a detailed schematic view of a concentrate mixing module of Figure 2;

Figure 5a is a detailed schematic view of an alternative arrangement of the concentrate mixing module of Figure 2;

Figure 5b is a detailed schematic view of an alternative arrangement of the concentrate mixing module of Figure 5a;

Figure 6 is a detailed schematic view of a drainage module of Figure 2;

Figure 7 is a detailed schematic view of a cycler and sterilisable connector module of Figure 2;

Figure 8 is a perspective view of a first example of a heat exchanger for use in the sterilising of PD fluid according to the invention;

Figure 9 is a perspective view of a second example of a heat exchanger for use in the sterilising of PD fluid according to the invention;

Figure 10 is a perspective view of a disposable concentrate container according to the invention;

Figure 11 is a partially sectional view through the disposable concentrate container of Figure 10 with a vertical section of a chassis removed;

Figures 12a to 12c are perspective views of portions of the disposable concentrate container of Figure 10;

Figure 13 is a perspective view of a compartment of the disposable concentrate container of Figure 10;

Figure 14 is a perspective view of a further compartment of the disposable concentrate container of Figure 10;

Figure 15 is a sectional view through the disposable concentrate container during fitting to the apparatus of the invention;

Figure 16 is a further sectional view through the disposable concentrate container during fitting to the apparatus of the invention;

Figure 17 is a sectional view through the disposable concentrate container in position on the apparatus of the invention;

Figure 18 is an alternative sectional view of the disposable concentrate container;

Figures 19a-19d are schematic views of a sterilisable connector of the apparatus of the invention;

Figure 20 is a schematic view of a disposable fluid line for use with the apparatus of the invention;

Figure 21 is a schematic view of a sampling disposable fluid line for use with the apparatus of the invention;

Figure 22 is a detailed sectional partial view of a compartment of the disposable concentrate container of Figure 10; and

Figure 23 is a sectional view through a glucose compartment of the disposable concentrate container of Figure 10.

Figure 24 is sectional view through a lactic acid compartment of the disposable concentrate container of Figure 10.

Figure 25 is sectional view through the lactic acid compartment of Figure 24 in an engaged position.

Description of the detailed embodiments

Figure 1 is a partially schematic perspective view of an apparatus 100 for the preparation of peritoneal dialysis fluid for a patient according to a first embodiment of the invention. The apparatus 100 is connected to a domestic water supply by means of a tap water connection 1 and is connected to the domestic sewerage system by means of an external drain connection 16. The external waste connection 16 may be in the form of a replaceable waste line. The apparatus 100 is powered by the domestic electricity supply via a mains electricity connection 20. Concentrated components of the PD fluid are supplied to the apparatus 100 in a concentrate disposable

container 402. The PD fluid is supplied to and drained from the patient's peritoneal cavity by a disposable fluid line 10 which forms a fluid connection between the patient and the apparatus 100.

The apparatus 100 receives details of a prescription of the PD fluid for the patient on a smart card 102 which is read by the apparatus 100. The apparatus 100 also includes a control panel 104 which displays information to the patient and allows the patient to control the operation of the apparatus in certain respects.

In overview, the apparatus 100 according to this embodiment of the invention is installed in a patient's home and purifies tap water from the tap water connection 1, mixes the purified tap water with concentrated PD fluid components from the concentrate disposable container 402 to produce PD fluid. The apparatus 100 then sterilises the PD fluid and delivers the PD fluid by way of the disposable fluid line 10 directly to the peritoneal cavity of the patient. During a treatment session, which comprises a series of fill and drain cycles, old PD fluid, dialysate, is removed and fresh PD fluid is added to the patient's peritoneal cavity, normally during the night while the patient is asleep.

The disposable container 402 may include a bar code 18 arranged on the container at a convenient position. A bar code reader 19 shown in broken lines, inside the apparatus 100 reads the bar code as the container is inserted in the apparatus.

Although the apparatus 100 is primarily intended for use in a patient's home, the apparatus 100 may be used in centres such as dialysis clinics and hospitals. The apparatus includes a control system (not shown) which monitors and controls the operation of the apparatus 100 during normal use. In addition to the control system, the apparatus 100 includes a protective system (not shown) which is separate from the control system and monitors the correct operation of the apparatus 100 independently of the control system to ensure that the patient's safety is not compromised. The control system and the protective system are able to carry out functional tests to ensure that they are operating correctly.

At the start of the treatment session, the user, for example the patient, is required to confirm some of the parameters of the intended treatment which are displayed on the control panel 104. Such parameters include, for example, the patient's name, the volume of PD fluid to be entered into the peritoneal cavity of the patient, the glucose concentration of the PD fluid or the expiry date of the disposable concentrate container 402. Some of these parameters are stored on the smartcard 102. This corresponds to the stage in traditional PD treatments where the patient compares the label on the plastic bag of PD fluid with the instructions given by the doctor. Also at the start of the PD treatment, the patient is required to identify himself to ensure that the apparatus is not operated by an unauthorised person.

At the end of a treatment session, the concentrate disposable container 402 is replaced and the old container is discarded. Similarly, the disposable fluid line 10 is also replaced at the end of the treatment session with a new line.

At the start of a treatment session, the patient can set the concentration of glucose required in the PD fluid for that treatment session, within predefined limits, according to the patient's requirements. The glucose concentration is set by the patient using the control panel 104. The glucose in the PD fluid acts as an osmotic agent, so that an increase in the glucose concentration will result in an increase in the volume of fluid drawn across the peritoneum of the patient during the PD treatment.

The apparatus 100 is suitable for continuous cycling peritoneal dialysis (CCPD), where the peritoneal cavity is filled and emptied of PD fluid in a cyclic sequence, usually during the night. The apparatus 100 is also capable of carrying out tidal peritoneal dialysis according to which the peritoneal cavity is initially filled with PD fluid and in subsequent cycles a volume less than the total volume of the initial fill is drained from the peritoneal cavity and replaced with an approximately equal volume of fresh fluid. The peritoneal dialysis treatment session may take place while the patient is asleep and thus the apparatus 100 is usually located adjacent

the patient's bed. Other treatment modes are also possible.

At the end of a treatment session, the peritoneal cavity of the patient may be left full of PD fluid or the PD fluid may be drained from the peritoneal cavity, depending on the patient requirements. In general, it is expected that the apparatus 100 will be the sole source of the patient's PD treatment. Thus, if at the end of a treatment session the patient's peritoneal cavity is full of PD fluid, it is expected that the cavity will be full of PD fluid at the beginning of the next treatment session. However, the patient may have drained or filled his peritoneal cavity manually using additional PD equipment between treatment sessions. The apparatus 100 is able to respond to such situations by having input means whereby the patient may enter relevant data to the apparatus.

In a usual treatment session, a total volume of about 8-25 litres of PD fluid is put into and removed from the patient's peritoneal cavity, with each fill volume being between 250 ml and 3 litres (the smaller volume may be in the case of tidal peritoneal dialysis, for example). One treatment session may involve up to 20 fill and drain cycles, with a maximum of 25 litres of PD fluid (50 litres if the disposable concentrate container 402 is changed) being supplied to the patient and a maximum of 35 litres of fluid (per container used) being drained from the patient, the drain volume being up to 4 litres per cycle.

The patient is able to instruct the apparatus 100 via the control panel 104 to abandon the treatment session and allow the patient to disconnect from the apparatus 100 or to finish the treatment session early by omitting some of the cycles within the treatment session.

The apparatus 100 includes a timer (not shown) which allows the patient to set the approximate time at which a treatment session should begin so that the apparatus 100 can make the necessary preparations for the treatment session before the patient arrives. Thus, when such a time has been set, treatment can begin less than 20 minutes, preferably less than 10 minutes, after the patient has arrived and has confirmed that a treatment session is actually required. If the

timer has not been preset, the apparatus 100 may require up to one hour to make the necessary preparations for the delivery of dialysis fluid.

The control panel 104 includes a 256 colour video touch screen display with a screen saver. The control panel allows the user, inter alia, to set the glucose level concentration of the PD fluid within preset limits, start, interrupt, resume, abandon or finish the treatment session, adjust the temperature of the dialysis fluid between 35°C and 40°C and set the planned start time for the next or subsequent treatment sessions. The control panel displays the treatment status and the time until the end of the treatment session during treatment or the time until the start of the treatment session during preparation for a treatment session. On request, the control panel 104 displays the treatment mode (for example tidal or continuous peritoneal dialysis), the number of cycles in the treatment session, the glucose concentration, the accumulated fill volume for the treatment session, the accumulated drain volume for the treatment session, the accumulated ultrafiltration volume for the treatment session, the fluid delivery temperature set point, patient identification information from the smartcard 102 or patient entered information, the status of the treatment session and technical error codes. The ultrafiltration volume is the difference between the volume of PD fluid supplied to the patient and the volume of PD fluid drained from the patient. The control panel is also able to display visual alarms and is provided with an audible alarm with which the apparatus 100 can bring the patient's attention to operating problems. The control panel 104 may also be arranged to display additional information for use by a nurse, such as service information and fill rates and volumes, provided that the nurse can provide a valid identification code.

The apparatus 100 can be interrogated by a service engineer using a laptop computer (not shown) either directly or via a remote connections such as a modem (not shown).

The smartcard 102 stores the patient's prescription and for each of the last 20 treatment sessions, the prescription, the ultrafiltration volume, the monitor identity, date and time

plus any variances between the prescribed and delivered treatment and the reasons therefor if known to the monitor. The smartcard 102 also stores patient identification information and the acceptable limits of patient-selected levels such as numbers of cycles and glucose concentration. The physical characteristics of the smartcard are similar to those used in the PD 200™ peritoneal dialysis system manufactured by Gambro AB of Lund, Sweden, although the apparatus 100 can differentiate between the PD 200 cards and cards suitable for use with the apparatus 100.

The information on the smartcard 102 can be altered by a doctor either by connecting a computer (not shown) with a suitable interface to the apparatus 100 or by inserting the smartcard 102 into a suitable card reader attached to a computer (not shown). Service personnel are also able to interrogate the apparatus 100 using a computer (not shown) and a data link directly to the apparatus.

Figure 1a shows a block diagram of a smart card reader 103 which is connected to an operating system processor 108 and a protective system processor 106. The processors operate and supervise the system in a manner previously known in the art of dialysis machines. The processors are also connected to the control panel 104. Processors 106 and 108 are associated with memory devices 110 and 112, such as volatile memory, static memory, hard disk, solid state memory devices etc.

The operating system processor receives data input from sensors and other means in the apparatus and output control signals for controlling processes in the apparatus such as valves and pumps.

The protective system processor receives data input from sensors and other means in the apparatus and output control signals for the purpose of supervising the operating system processor and other processes in the apparatus. The protective system sensors are separate from the operating system processor sensors.

Figure 2 shows schematically the fluid path in the apparatus 100 of Figure 1. The apparatus is, for ease of understanding, represented in terms of six interconnected

functional modules, which each perform a specific role in the preparation of the peritoneal dialysis fluid and the peritoneal dialysis treatment. These modules are: a water preparation module 200; a thermal control and sterilisation module 300; a concentrate mixing module 400; a drainage module 500; a cycler and sterilisable connector module 600; and a sampling module 700.

In the following, the overall structure of the fluid path in the apparatus 100 will be described and then further details of the individual modules will be given.

As used in this description the terms "cleaning", "disinfection" and "sterilisation" have distinct meanings: "cleaning" simply means the removal of deposits within the system; "disinfection" means the neutralisation of most bacteria; and "sterilisation" means the inactivation of all bacteria with a 1 in 10^6 confidence level, i.e. the theoretical probability of the presence of a viable microorganism is less than or equal to 10^{-6} (see United States Pharmacopoeia, 23rd Edition and European Pharmacopoeia 1997).

As shown in Figure 2, tap water from the domestic supply is provided to the water preparation module 200 via the tap water connection 1. The water preparation module 200 controls the supply of water to the other modules in the apparatus by switching the tap water supply on and off, by limiting the pressure of the water supply and by monitoring the availability of the water supply. The water preparation module 200 also reduces and controls the level of dissolved gas and chemical and bacteriological contamination in the water supplied to the concentrate mixing module 400. The water preparation module 200 is capable of operating with potable water as generally defined by the US Environmental Protection Agency in the drinking water standard of November 1996, at pressures from 1-6 bar gauge (100-600 kPa above atmospheric pressure) and at temperatures between 5 and 30°C.

The water preparation module 200 is connected to the thermal control and sterilisation module 300 via five fluid connections 2a-2e. A cooling water output connection 2a supplies softened, pressure-controlled water for use in the

cooling functions of the thermal control and sterilisation module 300. The temperature of the cooling water is raised in the thermal control and sterilisation module 300, due, at least in part, to the water being used for cooling purposes. In this way, the water returned to the water preparation module 200 is preheated to improve the efficiency of the water preparation module, using waste heat from other parts of the apparatus 100. The cooling water is returned to the water preparation module 200 from the thermal control and sterilisation module 300 via a cooling water return connection 2b at a controlled temperature of approximately 30°C.

Purified water prepared by the water preparation module 200 is passed to the thermal control and sterilisation module 300 via a purified water connection 2c. Waste water from the water purification process is passed from the water preparation module 200 to the thermal control and sterilisation module 300 for cooling via a purification waste connection 2d.

The water preparation module 200 vents excess gas to atmosphere via an isolator air vent 17. The water preparation module 200 is also able to vent air to and from the thermal control and sterilisation module 300 via a patient heat exchanger vent connection 2e.

For disinfection purposes the water preparation module 200 receives water at disinfection temperature from the concentrate mixing module 400 via a reverse osmosis (RO) membrane disinfection connection 3.

The water preparation module 200 has a connection for a disinfectant cartridge 210, which supplies chemical disinfectant for the disinfection of the water preparation module 200, when required.

The thermal control and sterilisation module 300 sterilises the PD fluid supplied to the patient, and provides a supply of sufficiently hot water for disinfection of the concentrate mixing module 400 and the drainage module 500.

The thermal control and sterilisation module 300 also controls the temperature of the water supplied to the water preparation module 200 via the cooling water return connection 2b and to the concentrate mixing module 400 via a mixing water

feed connection 4a. One important role of the thermal control and sterilisation module 300 is to prevent heat being wasted and to sequence heating operations, so that the apparatus does not require more power than can be supplied by a domestic electricity socket. The apparatus 100 is designed to operate with a mains electricity supply of either 90-140V, 10A, 50/60 Hz (for example in North America and Japan) or 198-253V, 10A, 50/60 Hz (for example in Europe). The maximum power consumption of the apparatus 100 is therefore between 0.9 kW and 2.5 kW. During filling of the patient with PD fluid, the power consumption is around 1.2 kW. If the electricity supply is unable to provide sufficient power to sterilise the PD fluid at a flow rate of 300 ml/min, the flow rate is reduced, for example to 150 ml/min, to reduce the power required to sterilise the PD fluid. The major part of the energy consumption of the apparatus 100 is required for heating of water and PD fluid for disinfection and sterilisation during filling of the patient.

The connections between the water preparation module 200 and the thermal control and sterilisation module 300 are described above. The thermal control and sterilisation module 300 also supplies temperature controlled purified water to the concentrate mixing module 400 via the mixing water feed connection 4a. The output, for example PD fluid, of the concentrate mixing module 400 is returned to the thermal control and sterilisation module 300 via a mixing module output connection 4b.

The fluid entering the thermal control and sterilisation module 300 at the mixing module output connection 4b passes through an input volumetric flow meter 350 which, when the apparatus is supplying PD fluid to the patient, measures the volume of fluid supplied to the patient. An output volumetric flow meter 650 is provided in the cycler and sterilisable connector module 600 and measures the volume of fluid removed from the patient. The change in the patient's body fluid level due to the PD treatment is calculated by subtracting the volume of fluid drained from the patient from the volume of fluid supplied to the patient. This change is called the

ultrafiltration volume (UF) and is measured in the range -4 litres to +10 litres over the treatment session to an accuracy of ± 66 ml (or 0.66% of the total fill volume, if greater), preferably ± 33 ml (or 0.33% of the total fill volume, if greater).

When treating the patient, sterile PD fluid is passed from the thermal control and sterilisation module 300 to the cycler and sterilisable connector module 600 via a sterile fluid connection 8a. During sterilisation of the cycler and sterilisable connector module 600, water at sterilisation temperature is passed from the thermal control and sterilisation module 300 to the cycler and sterilisable connector module 600 via the sterile fluid connection 8a and returned to the thermal control and sterilisation module 300 via a sterilisation output connection 8b. The sterilisation water is returned to the cycler and sterilisable connector module 600 after heat recovery by the thermal control and sterilisation module 300 via a sterilisation fluid return connection 8c.

The thermal control and sterilisation module 300 connects to the drainage module 500 via a thermal drain connection 13a, which is used to pass the waste water from the purification waste connection 2d to the drainage module 500 after heat recovery. During disinfection, fluid is passed at low pressure from the drainage module 500 to the thermal control and sterilisation module 300 for heat recovery via a heat recovery drain connection 13b. This fluid is returned to the drainage module 500 after heat recovery via a heat recovery drain return connection 13c.

The concentrate mixing module 400 mixes concentrated PD fluid to the required recipe and supplies the PD fluid, suitably diluted, to the thermal control and sterilisation module 300 for sterilisation. The concentrate mixing module 400 also supplies cleaning agent to downstream modules of the apparatus, and controls the venting of air from the fluid circuit, while keeping microbiological contamination to a minimum.

As explained above, purified water is supplied to the

concentrate mixing module 400 via the mixing water feed connection 4a from the thermal control and sterilisation module 300, and chemically controlled PD fluid is returned to the thermal control and sterilisation module 300 via the mixing module output connection 4b. The concentrate mixing module 400 also has an air vent connection 6 to atmosphere to allow filling and draining of the fluid system, and a mixing module drain connection 15, which is used to supply water at disinfection temperature to the drainage module 500. Water at disinfection temperature is also supplied to the water preparation module 200 via the RO membrane disinfection connection 3.

The PD fluid is prepared by the concentrate mixing module 400 from concentrated components of the PD fluid provided in a disposable concentrate container 402 which connects to a manifold 404 of the concentrate mixing module 400 and is enclosed by a manifold cap 406.

Turning now to the drainage module 500, this module controls the flow of fluid to the external waste connection 16 and provides the negative pressure required to drain the patient of dialysate (the fluid removed from the patient at the end of a PD treatment). The external waste connection 16 may be permanently connected to the domestic sewerage system or temporarily connected, for example clipped over a lavatory bowl. The drainage module 500 also closes the drain line to isolate the fluid system when necessary, and stops the flow from the water preparation module to allow disinfection. The maximum flow rate to the external waste connection 16 is 3 litres/min and the maximum temperature of the fluid passing through the external waste connection 16 is 85°C.

The majority of the connections to the drainage module 500 have been described in relation to the other modules of the apparatus. The remaining connections, to the cycler and sterilisable connector module 600, will be described below.

The cycler and sterilisable connector module 600 prevents PD fluid of unsafe chemical composition, temperature or pressure or non-sterile PD fluid from being passed to the patient 50, by closing off the appropriate supply lines. As

described above, the cycler and sterilisable connector module 600 is connected to the thermal control and sterilisation module 300 via the sterile fluid connection 8a, the sterilisation output connection 8b and the sterilisation fluid return connection 8c. The cycler and sterilisable connector module 600 connects to the patient 50 via a patient fill connection 9a and a patient drain connection 9b. The patient connections 9a,9b are made to a disposable fluid line 10 which is replaced by the patient 50 at the start of each PD treatment session and connects to the standard connector on the catheter (not shown) into the patient's peritoneal cavity. The disposable fluid line 10 is provided to the patient pre-sterilised and in a sterile package. The disposable fluid line 10, which may be seen in Fig. 19, 20 and 21, has a pierceable membrane 634 at the end that connects to the cycler and sterilisable connector module 600 and this membrane 634, in combination with a cap (not shown) on the catheter connector 654, maintains the sterility of the disposable fluid line 10 until it is used.

The cycler and sterilisable connector module 600 is arranged such that the fluid circuit from the sterile fluid connection 8a to the sterilisation output connection 8b which includes the pierceable membrane 634 at the end of the disposable fluid line 10 can be heat sterilised with water at sterilisation temperature from the thermal control and sterilisation module 300. The cycler and sterilisable connector module 600 maintains the sterility of the fluid circuit once the membrane 634 on the fluid line 10 has been pierced until the end of the treatment session, and also ensures that fluid can only be passed to the patient when intended.

The cycler and sterilisable connector module 600 has a negative pressure drain connection 14a to the drainage module 500 for draining the dialysate from the peritoneal cavity of the patient, and an ambient pressure drain connection 14b which is used to drain fluids other than the dialysate from the cycler and sterilisable connector module 600.

The sampling module 700 is connected to the disposable fluid line 10 via sampling interface 11 and collects a 15 ml

sample of dialysate, when requested, for analysis. The sample represents an average of the composition of the drained dialysate over all the cycles of the treatment session.

The structure of the individual modules will now be described in more detail with reference to the figures.

Water Preparation Module 200

Figure 3 shows in detail the structure of the water preparation module 200. Tap water from the domestic mains supply enters the water preparation module 200 through the tap water connection 1. The flow of mains water can be switched off completely by an inlet valve 202. From the inlet valve 202, the water passes through a 30 micron particulate filter 204 which protects the moving parts of the water preparation module 200 from coarse particles in the water supply. The filter 204 also prevents damage or blocking of the downstream components of water preparation module 200, such as reverse osmosis membranes or particle filters.

The filtered water passes through a water softener 206, for example in the form of an ion exchange column. Waste water from the water softener 206 produced during regeneration of the water softener 206 is passed to the drainage module 500 via a normally closed water softener valve 268, the purification waste connection 2d and the thermal drain connection 13a of the thermal control and sterilisation module 300. The water softener 206 protects the fluid components of the water preparation module 200, such as reverse osmosis (RO) membranes 238,252 from limescale which would degrade their performance. It is important for the operation of the RO membranes 238,252 that the supplied water is soft in order to prevent a build-up of limescale.

The softened water passes to an isolator 208, in the form of a tank equipped with a float valve, which prevents a back flow of material from the water preparation module 200 into the mains supply and also reduces the pressure of the water from mains pressure to atmospheric pressure. Air from the isolator 208 is directed to atmosphere at the isolator air vent 17, which can be opened and closed by an isolator air vent valve

209. The isolator 208 is also able to receive air from and pass air to the thermal control and sterilisation module 300 via the patient heat exchanger vent connection 2e.

Downstream of the isolator 208, a branch of the fluid path including the disinfection cartridge 210 connects to the main fluid path and will be described later. The softened water in the main fluid path passes from the isolator 208 to the thermal control and sterilisation module 300 via the cooling water output 2a and is used in the thermal control and sterilisation module 300 for cooling purposes and pre-heating before being returned to the water preparation module 200 via the cooling water return connection 2b at a controlled temperature of approximately 30°C. The raised temperature of the water due to the preheating in the thermal control and sterilisation module 300 reduces the power required to pump the water through the RO membranes and improves the effectiveness of the degassing operation described below.

The preheated water returning to the water preparation module 200, via the cooling water return connection 2b passes through a series of components 214-224 which remove dissolved gas from the water. These components are a proportioning valve 214, a degassing restrictor 216, an expansion chamber 218, a degassing pump 222 and a degassing chamber 224. In operation, water from the degassing chamber 224 is recirculated via the proportioning valve 214 through the degassing restrictor 216 by the degassing pump 222, which is a gear pump. The pressure drop in the water due to the degassing restrictor 216 causes dissolved gas in the water to be forced out of solution and begin to form bubbles in the water. The pressure drop due to the degassing restrictor 216 is a function of the flow rate there through, which is maintained constant by recirculation from the degassing chamber 224, at a flow rate set by the degassing pump 222.

The degassing chamber 224 includes a level sensor 225, such as an ultrasonic level sensor, which detects the level of the water in the degassing chamber 224. The level sensor 225 controls the operation of the proportioning valve 214 such that if the level of water in the degassing chamber 224 drops, the

proportioning valve 214 is adjusted to allow water from the cooling water return connection 2b to supplement the water recirculated by the degassing pump 222 until the water level in the degassing chamber 224 returns to the maximum level. The recirculated flow from the degassing chamber 224 is decreased to maintain the flow through the degassing restrictor 216 constant. In this way, any flow of water out of the degassing chamber 224 downstream towards the RO membranes 238,252 is replaced by a flow of water at the same rate from the cooling water return connection 2b. However, the flow rate through the degassing restrictor 216 remains constant regardless of the downstream flow rate from the degassing chamber 224 due to the operation of the proportioning valve 214. A constant flow of 900 ml/min through the degassing restrictor 216 gives a pressure drop of 800 mbar (80 kPa), which is sufficient for effective degassing.

The reduced pressure water passes from the degassing restrictor 216 to the expansion chamber 218 which slows the flow sufficiently that bubbles of gas initiated during the rapid pressure reduction in the restrictor combine and have time to increase in size. Some of the bubbles rise to the surface of the water in the expansion chamber 218 and form a small head space of gas in the expansion chamber 218. The expansion chamber is provided with a gas-pipe 219 which connects the headspace in the expansion chamber 218 to the fluid path between the expansion chamber 218 and the degassing pump 222, so that gas bubbles are entrained in the fluid drawn from the expansion chamber 218 by the degassing pump 222. The mixture of gas and water are drawn from the expansion chamber 218 by the degassing pump 222 and the pressure of the water is monitored by a degassing pressure sensor 220 to ensure that the pressure is sufficiently low for effective degassing. The degassing pump 222 pumps the gas and water into the degassing chamber 224 where the gas is vented to the isolator 208 at atmospheric pressure. The level sensor 225 in the degassing chamber 224 controls the fluid flow through the proportioning valve 214 as described above by opening the proportioning valve 214 to increase the proportion of the flow through the

degassing restrictor 216 directly from the cooling water return connection 2b when the water level drops due to water being drawn from the degassing chamber 224 by downstream components of the water preparation module 200. In this way, fluid continuity in the subsequent sections of the water preparation module 200 is ensured.

A bypass from upstream of the proportioning valve 214 directly to the degassing pressure sensor 220 under the control of a degassing bypass valve 226 is provided so that disinfection can take place without the pressure drop associated with the degassing restrictor 216.

The degassed water from the degassing chamber 224 is drawn by an RO pump 236 (Model Procon 1608, from Procon Products Div./Roehlen Industries, Ten, USA) through an incoming water conductivity meter 228 which, in combination with an incoming water temperature sensor 230, measures the conductivity of the water. Each conductivity measurement of the water (or the PD fluid) by the apparatus 100 of the invention is accompanied by a temperature measurement, as the measured conductivity of a solution varies with temperature. The conductivity measurements are compensated by reference to the temperature at which they are taken to provide an indication of the ionic concentration in the water (or PD fluid).

After the conductivity measurement, the water passes through an activated carbon filter 232, available from Gambro AB of Lund, Sweden as part No. K06735001, the purpose of which is to remove free chlorine from the water and to adsorb some organic contaminants. Chlorine in the water can damage the surface of the membranes of the RO membrane units 238,252.

Following the activated carbon filter 232 the water passes through a 5 micron particulate filter 234 which removes from the water any traces of carbon or other particulate matter not caught by the first filter 204 which could foul the RO membranes in units 238,252.

The filtered water is pumped by the high pressure RO pump 236, preferably a rotary vane pump, past the surface of a first membrane in a RO membrane unit 238 (Type HSRO/2521/FF from Dow Film Tech, USA) and through a first RO output restrictor 240 to

the drainage module 500 via the purification waste connection 2d and the thermal control and sterilisation module 300. The high pressure of the water passing over the surface of the membrane in the first RO membrane unit 238 causes some of the water to pass through the membrane in RO membrane unit 238 overcoming the osmotic counterpressure caused by the ions in the retained liquid, in a reverse osmosis process. The remaining water, which includes any impurities which were present in the water, passes through the first RO output restrictor 240 to the purification waste connection 2d. The first RO output restrictor 240 maintains the pressure across the first membrane in RO membrane unit 238 to ensure effective reverse osmosis.

A first RO differential pressure sensor 242 is provided to measure the differential pressure between the inflow to the first RO membrane unit 238 and the waste flow therefrom (before the first RO output restrictor 240), in order to detect fouling of the first RO membrane unit 238. If the membrane in RO membrane unit 238 begins to foul, the resistance of the membrane to the tangential flow between inlet and waste begins to increase. Due to the largely constant flow that is delivered from the RO pump, the pressure differential is increased. When the pressure differential increases by greater than say 0.5 Bar, which is sensed by a differential pressure sensor 242a and 242b, the membrane is considered fouled. If the membrane in the RO membrane unit 238 begins to foul, there is also a higher pressure drop across the membrane, which is sensed by pressure sensors 242a and 242c.

The first RO differential pressure sensor 242 is in the form of two cavities separated by a diaphragm with one cavity in fluid communication with a point before the first RO membrane unit 238, as indicated by circle 242a, and one cavity in fluid communication with a point on the waste water output of the first RO membrane unit 238 before the first RO output restrictor 240, as indicated by circle 242b, or after the membrane in RO membrane unit 238, as indicated by circle 242c. The differential pressure is measured by monitoring the deformation of the diaphragm towards one or the other cavity.

It is not necessary for the control system to measure the absolute pressure at the locations of the first RO differential pressure sensor 242a, as only the differential pressure is required to detect fouling of the first RO membrane in RO membrane unit 238.

The conductivity of the RO water which has passed through the first membrane in RO membrane unit 238 is measured by a first RO conductivity meter 246 in combination with a first RO water temperature sensor 248.

A first RO membrane bypass valve 250 is provided for use in the disinfection of the water preparation module 200, and its function will be described below.

A second RO membrane unit 252 (Type HSRO/2521/FF from Dow Film Tech, USA) is provided downstream of the first RO membrane unit 238. The use of two RO membrane units 238, 252 gives a much higher purity of water than would be the case with only one membrane unit and also gives additional security in the event that one membrane ruptures. When measured in terms of conductivity, the first RO membrane unit 238 filters out approximately 98% of impurities from the water pumped across it by the RO pump 236, and the second RO membrane unit 252 filters out 80% of the remaining 2% of impurities. The quality of water required by the apparatus 100 is very high and may be difficult to achieve consistently with a single RO membrane. If one of the RO membranes 238, 252 ruptures, the other membrane will continue to provide purified water for the short period of time before the fault is detected by the protective system and the apparatus 100 is stopped.

The waste water from the second RO membrane unit 252 passes through a second RO output restrictor 254 in the same way as for the first RO membrane unit 238, except that this waste water is recycled through a disinfectant selection valve 256 back to the input of the RO pump 236. This is possible because the waste water from the second RO membrane unit 252 is already reasonably pure as it has passed through the first RO membrane unit 238. This recycling improves the overall water usage efficiency of the apparatus. Typically, in operation of the apparatus a flow rate of 750 ml/min of water is drawn from

the degassing chamber 224 by the RO pump 236. This flow rate is supplemented by 250 ml/min of water recycled from the second RO membrane unit 252, so that 1000 ml/min of water is pumped towards the first RO membrane unit 238. Of this 1000 ml/min of water, 500 ml/min passes to the purification waste connection 2d and 500 ml/min of purified water passes through the first RO membrane unit 238 to the second RO membrane unit 252. At the second RO membrane unit 252, a flow of 250 ml/min of water passes through the membrane to the purified water connection 2c and a flow of 250 ml/min is recycled back to the input of the first RO membrane unit 238.

A second RO differential pressure sensor 258 is provided to measure the differential pressure between the inflow and the waste flow of the second RO membrane unit 252 to detect fouling. The operation is the same as described in connection with the first RO differential pressure sensor 242, and the second RO differential pressure sensor 258 is divided in two cavities, a first cavity 258a and a second cavity 258b or 258c.

A RO pressure relief valve 260 is provided between the inflow to the second RO membrane unit 252 and the waste outflow therefrom, in order to control the pressure of the water presented to the second RO membrane unit 252, and to avoid a pressure build-up as the output demand at the purified water connection 2c varies. It is noted that the output demand from the second RO membrane unit 252 varies from full output, for example 250 ml/min, to zero during certain periods and anything there between. If the output from the second RO membrane unit 252 becomes small or zero, relief valve 260 shunts water in parallel to the restrictor 254 to thereby maintain approximately the same operation conditions for the first RO membrane unit 238 as with full output. This operation also reduced water consumption.

A second RO conductivity meter 262 and a second RO temperature sensor 264 are provided at the output of the second RO membrane unit 252 to measure the conductivity of the output water, in order to ensure that the water has been sufficiently purified from ionic components. An output water pressure sensor 266 is provided downstream of the second RO temperature sensor

264 to measure the pressure of the water output via the purified water connection 2c to the thermal control and sterilisation module 300.

During disinfection of the water preparation module 200, the disinfectant selection valve 256 is opened to direct the waste flow from the second RO membrane unit 252 through the disinfection cartridge 210. The disinfection cartridge 210 contains a chemical disinfectant, such as an aqueous solution of peracetic acid (a widely approved disinfectant), which is diluted by the water flow. During disinfection, a disinfection valve 212 is opened, the mains valve 202 is closed and flow through the purification waste connection 2d is prevented by the drainage module 500. The float valve of the isolator 208 prevents any backflow through the water softener 206. The first RO membrane bypass valve 250 is opened so that the waste water from the first RO membrane unit 238 is returned to the output side of the first RO membrane unit 238 rather than passing to the drainage module 500 via the purification waste connection 2d, which is closed by the drainage module 500. Degassing bypass valve 226 is opened to allow fluid flow there through. It will be seen therefore that a closed recirculation loop is created for circulation of the chemical disinfectant through the water preparation module 200. This closed loop disinfects most of the components and fluid paths of the water preparation module 200. However, to disinfect the fluid path between the disinfectant selection valve 256 and the RO pump 236, the disinfectant selection valve 256 is closed so that disinfection fluid already in the fluid channel between the second RO restrictor 254 and the disinfectant selection valve 256 is circulated past the disinfectant selection valve 256 and through the RO pump 236.

A further recirculation path is provided from the gas output of the degassing chamber 224 through the isolator 208 and the degassing bypass valve 226, so that disinfection fluid is able to circulate through the isolator 208. The degassing bypass valve 226 is opened to allow fluid flow there through, so that the pressure of the disinfection fluid is not reduced by the degassing restrictor 216, which could cause the

peracetic acid to form hydrogen peroxide, thereby reducing its effectiveness. Likewise, in the case of hot water disinfection, the drop in pressure through the degassing restrictor 216 could cause the water to boil. Although the degassing bypass valve 226 is opened, a small portion of the disinfection fluid is still passed through the degassing restrictor 216 to disinfect this fluid path.

Once all components downstream of the water softener 206 have been disinfected, the disinfection fluid is passed to the drainage module 500 through the purification waste connection 2d.

Water at disinfection temperature is introduced into the output side of the second RO membrane unit 252 via the RO membrane disinfection connection 3 for disinfection of the components of the water preparation module downstream of the second RO membrane unit 252.

In the case of heat disinfection of the water preparation module 200, the disinfectant cartridge 210 is not required and the water is heated during disinfection by the thermal control and sterilisation module 200 between the cooling water output 2a and the cooling water return connection 2b.

Thermal Control and Sterilisation Module 300

Figure 4 shows in detail the structure of the thermal control and sterilisation module 300. Water from the cooling water output 2a of the water preparation module 200 is directed through a purification waste heat exchanger 324, where it is preheated by the water from the purification waste connection 2d passing through the purification waste heat exchanger 324 to the thermal drain connection 13a. The water heated by the purification waste heat exchanger 324 is heated by an electric water heater 322 before exiting the cooling water return connection 2b to ensure that it is at the optimum operating temperature for the water preparation module 200, normally 30°C.

In the thermal control and sterilisation module 300, water is circulated, in normal operation, by a patient output heat exchanger pump 316, in the form of a gear pump through a

patient output heat exchanger 314 and a recirculation restrictor 310. The patient output heat exchanger 314 is in the form of a bath of water through which the fluid from an online autoclave 375 (described later) passes in a sealed conduit. The bath is kept at a constant temperature by the recirculating water to maintain the PD fluid passed to the patient at the required delivery temperature. If the temperature of the recirculating water is too high, a patient output heat exchanger drain valve 318 is opened so that the heated water can pass out of the patient output heat exchanger 314 to the cooling water return connection 2b via a patient output heat exchanger drain restrictor 308 and the water heater 322. A corresponding amount of colder water is drawn from the cooling water output 2a of the water preparation module 200 by the patient output heat exchanger pump 316, until the temperature of the heating bath of the patient output heat exchanger 314 has been reduced to the desired level

When it is not desired to extract heat from the patient output, for example because the patient output fluid lines are being sterilised at high temperature, the patient output heat exchanger 314 is drained under the influence of gravity by opening the patient output heat exchanger drain valve 318 and an air bleed valve 320. Air enters the patient output heat exchanger 314 through the patient output heat exchanger vent connection 2e from the isolator 208 via the opened air bleed valve 320 and an air bleed restrictor 312. When the patient output heat exchanger 314 is full of air, rather than water, negligible heat is transferred to or from the patient output fluid. In this case, the patient output heat exchanger pump 316 is inactive. The patient output heat exchanger 314 is refilled by opening the air bleed valve 320 to vent the air and reactivating the patient output heat exchanger pump 316 with the patient output heat exchanger drain valve 318 closed.

The purified water produced by the water preparation module 200 is passed to the thermal control and sterilisation module 300 via the purified water connection 2c. The purified water passes through a disinfection heat exchanger 326 which is used during disinfection of the concentrate mixing module 400

to preheat the purified water by recovering heat passing from the heat recovery drain connection 13b to the heat recovery drain return connection 13c. The preheated water exiting the disinfection heat exchanger 326 is heated to disinfection temperature by an electric disinfection heater 330. During normal operation of the apparatus, the disinfection heater 330 is used to control the temperature of the water exiting the mixing water feed connection 4a to the concentrate mixing module 400.

During disinfection of the drainage module 500, water from the purified water connection 2c bypasses the disinfection heat exchanger 326 via a disinfection heat exchanger bypass valve 328, so that the water exiting the heat recovery drain return connection 13c remains at the disinfection temperature of 85°C. The disinfection heat exchanger bypass valve 328 is only used during disinfection of the drainage module 500.

The PD fluid produced by the concentrate mixing module 400 is passed to the thermal control and sterilisation module 300 via the mixing module output connection 4b. This fluid passes through the input volumetric flow meter 350 which records the flow of PD fluid filled into the patient. The PD fluid is drawn by a gear-type, volumetric pump 352 which is monitored by a tachometer 354 to ensure that the pump is operating at the expected volume flow rate. The delivery rate of the volumetric pump 352 is also monitored independently by the input volumetric flowmeter 350 to ensure correct operation. The volumetric pump 352 delivers the PD fluid at the required rate and pressure for on-line autoclaving, i.e. 300 ml/min and 6 bar absolute (600 kPa) to prevent the fluid from boiling at 150°C. A gear type pump has been selected to ensure that the water passing through the online autoclave 375 can be pressurised by the pump to the pressure necessary for the water to be heated to sterilisation temperature.

In normal operation of the apparatus 100, the PD fluid passes into the on-line autoclave (OLA) 375 through an OLA input valve 356. At this point, the pressure of the PD fluid is monitored by two independent OLA pressure sensors 358. One of the OLA pressure sensors 358 provides a pressure reading to the

control system for the apparatus, the other sensor provides a reading to the separate protective system, see Figure 1a, which ensures that, even in the event of the apparatus malfunctioning, patient safety is not compromised. The pressure, temperature and conductivity sensors which are positioned to monitor parameters that are crucial to the patient's safety in the system are all duplicated in this manner, so that the patient is never endangered by a single sensor malfunction and each patient safety measurement is independently double-checked.

Downstream of the OLA pressure sensors 358 the PD fluid passes through a first OLA heat exchanger 360 and a second OLA heat exchanger 362, both of which preheat the PD fluid entering the OLA heating bath 364 by recovering heat from the fluid exiting the OLA heating bath 364. The OLA heating bath 364 is an oil heating bath heated by an electric heater 365 and provided with a recirculation pump 366 (gear pump) and a heating bath temperature sensor 368. The oil or ethylene glycol is circulated by the recirculation pump 366 through a heating fluid path 367 which includes the oil bath and the PD fluid (or water) passes through a sterilisation fluid path 369. The heating fluid path 367 and the sterilisation fluid path 369 are separated by a thermally conductive barrier.

In order to ensure that the liquid leaving the OLA heating bath 364 is sterile, a parameter is defined which represents a sterilising value for the sterilisation process and which can be calculated, for example, from an algorithm modelling the temperature distribution inside the OLA heating bath 364, and from the value of at least one other parameter which influences the sterilisation treatment, namely the flow rate Q of the liquid to be sterilised in the OLA heating bath 364, the temperature (T_{in}) of the liquid to be sterilised entering the OLA heating bath 364 and the temperature (T_{Hin}) of the heating liquid (ethylene glycol) entering the OLA heating bath 364. Since the temperatures at the outlet of the OLA heating bath 364 (temperature of the sterilised liquid and temperature of the heating liquid) are linked to the temperatures at the inlet of the OLA heating bath 364, it is

also possible to take into account in the calculations the temperature (T_{out}) of the sterilised liquid leaving the OLA heating bath 364 and/or the temperature (T_{Hout}) of the heating liquid leaving the OLA heating bath 364.

When the parameter representing the sterilising value for the treatment is defined, a set value for this parameter is then chosen which is both high enough to correspond to an effective sterilisation of the liquid, and as low as possible in order to prevent or limit the degradation of the liquid to be sterilised when this liquid is heat-sensitive (as in the case of solutions for peritoneal dialysis which contain glucose).

During functioning, the control system of the apparatus 100 is programmed to calculate, at regular intervals, the value of the parameter representing the sterilising value for the treatment, from the algorithm of temperature distribution in the OLA heating bath 364, and the temperature and flow rate data measured by the OLA temperature sensors 370, the heating bath temperature sensor 368 and the input volumetric flowmeter 350. Each time that a new value for the parameter is calculated, the control system checks that this calculated value is higher than the set value and therefore confirms that the liquid is sterile. A further temperature sensor 379 is used for obtaining the temperature of the liquid to be sterilised by the OLA before entering the heat exchanger.

This checking process, which allows validation of the effective sterilisation of the liquid, can be passive. The reason for this is that, given that the sterile state is a crucial characteristic of the PD fluid it is possible to envisage a standard operating mode for the OLA 375 in which the choice of the flow rate for the liquid to be sterilised is limited to a restricted number of different predetermined values (for example three) and in which all of the other operating parameters for the device are preset as a function of the predetermined flow rates, such that the functioning of the device is simplified as much as possible. In this case, the checking process described above is used merely to validate the sterilisation.

It is also possible to envisage an operating mode for the OLA 375 in which the choice of flow rate of liquid to be sterilised is free within a range of determined values. In this case, the control system calculates, from the chosen flow rate and from the set value for the parameter representing the sterilising value, the other operating parameters for the device, in particular the temperature of the heating liquid as measured by temperature sensor 368. During functioning, the control system regularly adjusts the flow rate of the volumetric pump 352 and/or the temperature of the heating liquid circulated by the recirculation pump 366, such that the calculated value of the parameter is always greater than the set value.

The parameter denoted in the literature (see page 288 of the European Pharmacopoeia 1997, or page 1977 of the United States Pharmacopoeia, 23rd Edition) as F_0 (expressed in minutes) is used as the parameter representing the sterilising value for the sterilisation process. F_0 is the sum of the cumulative sterilising effects during a sterilisation treatment, or sterilising value F^Z_T when the reference temperature T is equal to 250°F (121.1°C) and the thermal inactivation value Z is equal to 18°F (10°C). The thermal inactivation value Z is the temperature increase which multiplies by ten the rate of destruction of a specific microorganism. Z = 10°C corresponds to a theoretical microorganism which is slightly more resistant than the microorganism reputed to be more heat-resistant than any other spore-forming microorganism, *Bacillus stearothermophilus*. The canonical formula for F_0 is shown in Equation 1.

$$F_0 = \int_0^t 10^{\left(\frac{T-121}{10}\right)} dt \qquad (1)$$

This formula cannot be applied directly to the checking of a sterilisation treatment in which the liquid to be sterilised is permanently flowing and in which the heating means used to raise the temperature of the liquid to be sterilised does not bring this liquid to the same temperature at all points in the heating chamber.

When the heating means is arranged to heat the liquid to be sterilised along a portion of the pipe in which the liquid is circulating, it is the believed that the formula shown in Equation 2 can be used to calculate F_0

$$F_0 = \int_0^L \frac{S}{Q} \times 10^{\left(\frac{T(y)-121}{10}\right)} dy \qquad (2)$$

In equation 2:

L = length of the sterilisation fluid path 369 of the liquid to be sterilised through the OLA heating bath 364;

S = internal cross section of the sterilisation fluid path 369 through the OLA heating bath 364;

Q = flow rate of the liquid to be sterilised through the OLA heating bath 364;

T(y) = equation of the temperature distribution of the liquid as a function of the distance from the inlet of the OLA heating bath 364.

The equation T(y) depends on the structure of the OLA heating bath 364 and on its operating mode. For example, Figure 8 shows a first example of a heat exchanger which is adapted for use in the OLA 375. This exchanger consists of two concentric pipes, the outer pipe forming a sleeve around the inner pipe. The sterilisation fluid path 369 is provided by the interior of the inner pipe and the heating fluid path 367 is provided between the inner and outer pipe.

During operation, the liquid to be sterilised and the heating liquid, for example ethylene glycol, are circulated, in opposite directions, in the inner pipe (sterilisation fluid path 369) and in the outer pipe (heating fluid path 367). The inside diameter of the sterilisation fluid path 369 is chosen such that, in the range of flow rates which includes the flow rates for operating the OLA 375 (100 to 400 ml/min), the flow of the liquid to be sterilised is always turbulent.

For an exchanger with an inner pipe made of stainless steel and an outer pipe made of copper and having the dimensions set out in Table 1 the equation for T(y) can be written according to Equation 3.

Table 1

Length (cm)	222
Inner pipe volume (ml)	26
Outer pipe volume (ml)	105
Cross section of the inner pipe (cm^2)	0.117
Area of the annular space between the inner and outer pipes (cm^2)	0.502
Internal perimeter of the inner pipe (cm)	1.213
External perimeter of the inner pipe (cm)	1.995
Internal exchange area of the inner pipe (cm^2)	269
External exchange area of the inner pipe (cm^2)	443

$$T(y) = T_{in} + (T_{Hin} - T_{in}) \times \frac{r \times [e^{-ny} - e^{-nL}]}{1 - r \times e^{-nL}} \qquad (3)$$

T_{in} = temperature of the liquid to be sterilised entering the sterilisation fluid path 369;

T_{Hin} = temperature of the heating liquid entering the heating fluid path 367 (such as measured by the heating bath temperature sensor 368).

$$r = 6 \times 10^{-5} \times Q^2 - 0.0577\ Q + 19.084$$

$$n = -\frac{1}{L} \ln\left[\frac{301415 - 958.18Q + Q^2}{292.6 + 65.72Q - 0.200453Q^2 + 0.00020948}\right]$$

Q = flow rate of the liquid in the sterilisation fluid path 369.

As emerges from this example, it is possible to calculate the sterilising value F_0 at any moment, from a measurement of the temperature T_{in} of the liquid to be sterilised entering the

OLA heating bath 364, a measurement of the temperature T_{Hin} of the heating liquid entering the OLA heating bath 364, a measurement of the flow rate Q of liquid to be sterilised and an equation modelling the temperature distribution inside the OLA heating bath 364.

In the preferred embodiment of the invention, as shown in Figure 4, the OLA heating bath is in the form of a bath of ethylene glycol which is agitated by the recirculation of the ethylene glycol by the recirculation pump 366 to ensure a uniform temperature throughout the OLA heating bath 364. The sterilisation fluid path 369 passes through the OLA heating bath 364 in a sealed conduit. The above principles are, however, applicable to the embodiment shown.

Throughout all the operating phases of the OLA 375 in which the OLA 375 is expected to produce a sterile liquid (water or PD fluid), the control system validates the sterilisation treatment carried out by checking that the calculated sterilising value F_o is always greater than a first threshold value F_{omin1} corresponding to the sterility of the liquid.

The OLA heating bath 364 heats the PD fluid to a temperature of greater than 150°C and maintains the PD fluid at this temperature for at least 2 seconds to autoclave the PD fluid and thereby ensure sterility. The flow rate through the OLA heating bath 364 is 300 ml/min. Under these conditions it is believed that the equivalent theoretical F_o value is at least 20 minutes.

The temperature of the sterile PD fluid exiting the OLA heating bath 364 is checked by two independent OLA temperature sensors 370 which ensure that the required temperature has been reached. Most of the heat from the autoclaved PD fluid is recovered to the PD fluid entering the OLA heating bath by the first and second OLA heat exchangers 360, 362. Any residual heat is recovered in the patient output heat exchanger 314 which ensures that the temperature is acceptable for the patient, i.e. 37°C. The temperature of the autoclaved PD fluid is checked downstream of the patient output heat exchanger 314 by two independent patient output temperature sensors 372.

Finally, the pressure of the PD fluid is reduced by a patient output pressure relief valve 374 to a safe pressure for delivery to the patient. The autoclaved, pressure and temperature controlled PD fluid is then passed to the cycler and sterilisable connector module 600 via the sterile fluid connection 8a.

During sterilisation of the cycler and sterilisable connector module 600 the fluid pumped by the volumetric pump 352 takes a different path through the OLA so that the fluid is at 130°C, rather than 37°C. The fluid is maintained at a pressure of 3 bar absolute (300 kPa) to prevent boiling. In this case, the fluid passes through an OLA sterilisation valve 376 and through a sterilisation heat exchanger 378 which recovers heat passing from the sterilisation output connection 8b of the cycler and sterilisable connector module 600 to the sterilisation fluid return connection 8c. The heat recovered by the sterilisation heat exchanger 378 is used to preheat the fluid, which then passes to the second OLA heat exchanger 362 for further preheating. The heating of the sterilisation fluid by the OLA heating bath 364 is similar to the process for autoclaving the PD fluid. However, heat is only recovered by the second OLA heat exchanger 362 and not the first OLA heat exchanger 360 or the patient output heat exchanger 314. The patient output heat exchanger 314 has been drained at this stage so that it contains only air which is a poor conductor of heat and does not therefore transfer a significant amount of heat from the sterilisation fluid. There is no flow through the heat-receiving side of the first OLA heat exchanger 360 because the OLA input valve 356 is closed and heat will not therefore be transferred to the heat-receiving side of the first OLA heat exchanger 360 once the fluid in that side has reached the temperature of the fluid in the heat transferring side. Even though there is no flow, the fluid in the heat-receiving side of the first OLA heat exchanger 360 does not boil because it is in communication with the fluid flow through the OLA heating bath 364 and is therefore at the same pressure. Thus, the fluid for sterilisation which exits the sterile fluid connection 8a has a much higher temperature, 130°C, than the fluid which is

provided to the patient, and is therefore suitable for sterilising the cycler and sterilisable connector module 600.

The sterilisation of the cycler and sterilisable connector module 600 is considered as effective when all of the points in the fluid circuit downstream of the OLA heating bath 364 have been brought, by means of the sterile liquid, to a minimum temperature T_2 for a minimum period t_2, which corresponds to a second set sterilising value F_{0min2}, given by Equation 4

$$F_{0min2} = t_2 \times 10^{\left(\frac{T_2 - 121}{10}\right)} \qquad (4)$$

Validation of the sterilisation of the fluid circuit can be achieved simply by the control system checking that, during an uninterrupted interval at least equal to t_2, the temperature of the liquid measured by the patient output temperature sensors 372 has constantly been above T_2.

Since the sterilisation of the cycler and sterilisable connector module 600 is to be carried out with sterile water, the control system must validate both the sterilisation of the liquid and sterilisation of the fluid circuit. In other words, the control system must check both that the sterilising value for the sterilisation treatment applied to the liquid is greater than F_{0min1} and that the sterilising value for the sterilisation treatment applied to the circuit is greater than F_{0min2}. For this reason, the second OLA heat exchanger 362 is used, as the temperature of the sterile liquid must be brought down from the fluid sterilisation temperature of 150°C (necessary to achieve F_{0min1}) to the circuit sterilisation temperature of 130°C (which is lower than 150°C so that the pressure required in the cycler and sterilisable connector module 600 is only 3 bar absolute rather than 6 bar absolute).

The patient output pressure relief valve 374 operates during sterilisation to maintain the fluid before the relief valve 374 at a high pressure of 6 bar absolute and the pressure after the relief valve at the high pressure of 3 bar absolute required to prevent boiling at 130°C. A skilled person realises how to construct such a valve. If the water began to boil, it

would not be possible to validate the sterilisation of the circuit, since it would not be possible to certify that every point of the circuit has come into contact with water at a minimum temperature for a minimum uninterrupted period of time.

The fluid path in the apparatus 100 is carefully insulated to prevent heat loss during disinfection and/or sterilisation. In particular, the relative locations of the hot components are chosen to ensure that heat loss is kept to a minimum, i.e. adjacent components keep each other warm. In this way, it is ensured that the fluid paths are maintained at the correct disinfection or sterilisation temperatures along the whole of the path. A temperature sensor 380 arranged at connection 8b may be used for verifying the sterility of the fluid circuit up to heat exchanger 378.

The heat exchangers 360,362,378 are in one embodiment shaped like the exchanger represented in Figure 9, i.e. with the junction on a part of their length of the heating pipe and the fluid pipe. The two portions of joined pipes are shaped to form a coil with joined spirals, and both the inside and the outside of the cylinder thus formed are covered with a material which is a good heat conductor.

Other details of the thermal control and sterilisation module 300 are described in our co-pending application entitled "Process and device for sterilising and dispensing a liquid for medical use", Gambro reference HP 1310, which is incorporated herein by reference and a copy of which is attached hereto.

Concentrate mixing module 400

Figure 5 shows in detail the structure of the concentrate mixing module 400. The concentrate mixing module 400 includes the disposable concentrate container 402 which interfaces with the manifold 404 and is covered by the manifold cap 406. The disposable concentrate container 402 includes chambers, in the form of compartments for an aqueous solution of lactic acid 408, cleaning agent 410 (for example powdered sodium carbonate), powdered sodium bicarbonate 412, powdered sodium chloride 414, powdered calcium chloride 416, powdered magnesium chloride 418 and powdered glucose 420. The disposable

concentrate container 402 contains enough material in each compartment for a PD treatment session of the patient according to a selected one of a large number of prescriptions.

The range of composition for each of the components of the PD fluid which can be delivered to the patient stored in the disposable concentrate container 402 is set out in Table 2, together with the composition range for sodium lactate which is formed from the lactic acid and sodium bicarbonate. The mass of the components in the disposable concentrate container 402 and the approximate volume of each compartment 408-420 are also given in Table 2.

Table 2

Component	Composition Range	Mass in compartment	Approx. volume of compartment
Sodium chloride	120-140 mmol/l	208g	300 ml
Magnesium chloride	0.25-0.50 mmol/l	36g	150 ml
Calcium chloride	1.0-2.0 mmol/l	52g	300 ml
Sodium lactate	0-40 mmol/l*	-	-
Sodium bicarbonate	0-40 mmol/l*	120g	150 ml
Lactic acid	Compatible with sodium lactate and sodium bicarbonate levels	120g	300 ml
Glucose	1.5-4.0% w/w	1176g	1800 ml
Sodium carbonate	-	20	150 ml

Note: *In any given solution, the molar concentrations of sodium lactate and sodium bicarbonate add up to between 30 and 40 mmol/l.

The concentration of sodium in the PD fluid delivered to the patient is within ± 2.5% of the requested amount. The concentration of each of the other ingredients is within ± 5% of the requested amount. This assumes a fill volume of at least one litre. It is likely that for any given prescription, at least one of the components of the dialysis fluid in the container 402 will not be entirely used up, as the amounts are selected to cover a wide variety of prescriptions.

In addition or as an alternative to the components listed in Table 2, other components could be included, for example potassium salts.

It should be noted that the relative arrangement i.e. the order, of the compartments 408-420 in Figure 5 (and Figure 5a) is schematic only, and does not represent any physical order, but is chosen to easily represent the topology of the fluid system. Figures 10 and 11 show the order of the compartments 408-420 in the disposable concentrate container 402 according to one embodiment of the invention.

Figure 10 shows the construction of the disposable concentrate container 402. The compartments 408-420 are individually injection moulded in polypropylene and are mounted to a chassis 401 at their lower ends. The upper ends of the compartments 408-420 are held together by a lid 403 which also serves to close off the upper end of the glucose compartment 420 and provide a carrying handle for the container 402. As is clear from Table 2, the lactic acid compartment 408, the sodium chloride compartment 414 and the calcium chloride compartment 416 are each approximately twice the volume of the cleaning agent compartment 410, the sodium bicarbonate compartment 412 or the magnesium chloride compartment 418. The glucose compartment 420 is significantly larger than the other compartments 408-418. Each of the compartments 408-418 is provided at its lower end with at least one connector 407 for connection to the manifold 404.

Figure 11 shows a partially sectional view through the disposable concentrate container 402 with part of the chassis 401 removed, and which clearly shows the connectors 407 of the

compartments 408-420. The glucose compartment 420 is provided with two connectors 407a, 407b, the function of which will be explained below.

Figures 12a to 12c show perspective views of the lid 403 (Figure 12a), glucose compartment 420 (Figure 12b) and chassis 401 (Figure 12c) of the disposable concentrate container. As shown in Figures 12a to 12c, the lower surface of the glucose compartment 420 is sloped to direct the glucose powder in the compartment 420 towards the input connector 407a. The connectors 407 of each of the compartments 408-420 are received in corresponding holes 409 defined in the chassis 401. The holes 409 are aligned in the longitudinal direction of the chassis 401 along a line A which is offset by a distance from the longitudinal axis of symmetry B of the chassis 401. In this way, the container 402 is made rotationally asymmetric so that it cannot be inserted into the apparatus 100 the wrong way round.

The compartments 408-418 are snapped in place and the glucose compartment 420 is hot rivetted (heat staked) to the chassis 401 using rivets 411 which are formed integrally with the compartment 420. The rivets 411 are received in corresponding holes 405 in the chassis 401. Also, the rivets 411 of compartments 408 to 418 may be hot rivetted.

The chassis 401 includes a skirt 413 which is corrugated for strength and protects the connectors 407 when the container 402 is placed on a surface. The skirt or the connectors may be provided with a removable strip 443 for the protection of the connectors 407 during transport and storage.

Figure 13 shows the magnesium chloride compartment 418 as an example of the smaller size of compartment 410,412,418. Figure 14 shows the sodium chloride compartment 414 as an example of the larger size of compartment 408,414,416. The lower surface of each size of compartment 410,412,418 and 408,414,416 slopes towards the connector 407 so that the powder (or liquid) in the compartment 408-418 is directed towards the connector. Each compartment 408-418 has a compartment lid 415 which is fitted to the compartment 408-418 after the compartment has been filled with the respective powder or

liquid. In this way, it is not necessary to fill the container 408-418 through the narrow connector 407, which would be difficult. The compartment lids 415 are heat welded (hot melted) to the respective compartments 408-418. As mentioned above, the container lid 403 also forms the lid which closes off the glucose compartment 420 and is heat welded thereto.

Referring back to Figure 5, a new disposable concentrate container 402 is connected to the manifold 404 at the beginning of a PD treatment session, after disinfection, and is disconnected and discarded once the treatment has finished. A connection motor 422 engages with the disposable concentrate container 402 and drives the container into connection with the manifold 404.

Functionally, the compartments 408-420 of the disposable concentrate container 402 are of three types. The first type includes the lactic acid compartment 408, the cleaning agent compartment 410, the calcium chloride compartment 416 and the magnesium chloride compartment 418. This first type of compartment has an air vent channel 424 which extends from an upper region of the interior of the compartment to a direct opening to atmosphere in the manifold 404 when the compartment 408,410,416,418 is connected to the manifold 404. The air vent channel 424 allows air to exit the compartment 408,410,416,418 when water is introduced into the compartment via a fluid channel 426 of this type of container or when fluid is withdrawn from the compartment 408,410,416,418 via the fluid channel 426. The fluid channel 426 introduces the fluid in a lower region of the interior of the compartment 408,410,416,418 so that the water contacts all of the material as the water level rises up the compartment.

This first type of compartment 408,410,416,418 is used to contain powdered salts which are only required in small amounts, so that the salt can be included in an amount which dissolves completely without additional agitation when a sufficient amount of water is introduced into the compartment, or for salts which are already in a concentrated solution.

The second type of compartment 412,414 is used for salts which are required in such large volumes that the compartment

412,414 would have to be too large to contain at once all of the water required to dissolve all of the required salt. Thus, compartment 412 contains sodium bicarbonate and compartment 414 contains sodium chloride. This type of compartment includes a combined air vent and fluid channel 428 and a combined priming and output channel 430. Initially the salt in this type of compartment 412,414 is immersed (or primed) by introducing water through the combined priming and output channel 430 in a lower region of the compartment, while air is vented from an upper region of the compartment through the combined air vent and fluid channel 428. The priming operation fills the compartment 412,414 with water to immerse all of the salt therein. A similar technique is described in EP-A-0278100 which is incorporated herein by reference.

Once the salt has been fully wetted, water is drawn through the combined air vent and fluid channel 428 and allowed to percolate through and dissolve the salt, so that salt solution can be drawn off in a lower region of the compartment 412,414 through the combined priming and output channel 430. As the salt solution is drawn from the compartment 412,414 the reduction in pressure causes a corresponding volume of water to enter the compartment 412,414 through the combined air vent and fluid channel 428 which is connected to a source of water.

It would be possible to operate the second type of compartment 412,414 in a similar manner to the first type of compartment 408,410,416,418. For example, the compartment may be filled with water through the output channel 430 to dissolve the salt therein and the (substantially saturated) salt solution may be withdrawn through the output channel 430. Because the amount of salt in the second type of compartment 412,414 is larger than can be dissolved by the volume of water that fills the compartment 412,414, some salt will remain in the compartment 412,414 after the solution is withdrawn. The compartment 412,414 can therefore be refilled with water to obtain more solution.

The physical configuration of the first and second types of compartment is identical when the container 402 is not connected to the manifold 404. It is only the contents of the

compartment and the arrangement of valves and air vents in the mixing module 400 which determines the type of the compartment.

The third type of compartment is the glucose compartment 420. Glucose is particularly difficult to dissolve consistently and quickly in high concentrations, such as 50%, and therefore requires recirculation to ensure that all the glucose is dissolved. Furthermore, the volume of the glucose solution decreases as the glucose dissolves and thus the glucose compartment 420 requires continuous venting throughout the dissolution process. Thus, the glucose compartment 420 includes a glucose air vent channel 432 which is permanently connected to atmosphere when the disposable concentrate container 402 is connected to the manifold 404, a fluid input channel 434 which inputs water or recirculated glucose solution to a lower region of the glucose compartment 420, and a glucose output channel 436 which draws glucose solution from an upper region of the glucose compartment 420 through a glucose particle filter 438 which prevents particles of glucose from accidentally entering the fluid system.

The inventors have found that good results are achieved with monohydrate glucose, specifically LYCADEX PF/Dextrose mono pyrogen free from Roquette Freres S.A. of Lestrem, France, because this glucose is available in the quality required by the European Pharmacopoeia 1997 and is relatively inexpensive. Furthermore, the inventors have found that anhydrous glucose forms a cake when water is added to it which prevents effective dissolution. It is believed that a relatively large particle size is also advantageous in terms of effective dissolution, since large particle size results in improved flowability and less caking.

Figure 15 shows a sectional view through the lower part of the glucose compartment 420 of the disposable concentrate container 402 in position above the manifold 404, which illustrates the relative positions of the container 402, cap 406 and manifold 404 when the container 402 is loaded into the apparatus 100. The container 402 is loaded into the apparatus 100 by sliding it horizontally along a pair of container support rails 417. The container support rails 417 engage with

projections 419 on the connectors 407 of the container 402 so that the container support rails 417 hold the container 402 in a vertical position. The container support rails 417 are driven by the connection motor 422, see Fig. 5, in the vertical direction to raise or lower the container 402. It should be noted that when the disposable concentrate container 402 is loaded into the apparatus 100, the cap 406 closes off the manifold 404 to prevent outside contamination of the manifold 404 while the interior of the apparatus 100 is necessarily open to the atmosphere. Once the container 402 is loaded into the apparatus 100, the connection motor 422 acts to drive the container 402 downwardly via the container support rails 417 onto the cap 406 to keep the cap 406 firmly in position on the manifold 404 during disinfection.

As shown in Figure 15, the manifold 404 includes a drainage port 441 through which fluid may be drained to a reservoir vent disinfection valve 498, as described below.

As shown in Figure 15, the connector 407 includes an insert 421 which fits inside the neck of the compartment 420 and retains a septum 423 of silicone rubber or thermoplastic elastomer which seals off the compartment 420 during storage. The insert 421 includes (part of) the projections 419 for engagement with the container support rails 417 and is welded into the neck of the compartment 420. The connectors 407 of each of the compartments 408-420 are all constructed in the same manner.

Within the compartment 420, a central pipe 425 runs up to the top of the compartment 420, although this is not shown in Figure 15. Each compartment 408-420 has a central pipe 425 which functions as the air vent channel 424, the combined air vent and fluid channel 428, the glucose output channel 436 or the glucose air vent channel 432 depending on the particular compartment 408-420.

At its upper end (not shown) the central pipe 425 may be received in an annular projection from the compartment lid 415 which is of a larger diameter than the central pipe 425 and circumscribes the central pipe 425. The gap between the annular projection and the wall of the central pipe 425 may act as a

filter.

Alternatively, the central pipe 425 may be provided with an injection moulded filter element 439 as shown in Figure 23.

Between the base of the central pipe 425 and the sloping floor of the compartment 420, a diffuser 427 is provided in the form of a series of spaced bars extending radially outwardly from the central pipe 425 to the floor of the compartment 420. The diffuser 427 is shown in more detail in Figure 22. The diffuser 427 supports the central pipe 425 in the compartment 420 and also diffuses the flow of water (or other fluid) into the compartment 420 so that the flow is turbulent which agitates the powdered salt (or glucose) in the compartment 420 to aid dissolution. When the turbulent flow of water dissolves the powder in the region of the diffuser 427 the remaining powder falls down inside the compartment 420 so that all of the powder is dissolved.

In general, each of the compartments 408-420 is constructed in this way. In one possible arrangement (not shown) the glucose compartment 420 has tapered sides extending outwardly in the upward direction which prevent the glucose powder in the compartment from lifting up when water is added. If there is a tendency for the powder to lift, a water channel is formed at the periphery of the compartment. The water dissolves any powder in this region, resulting in that the powder falls down and seals the channel.

As shown in Figure 15, the manifold 404 comprises a respective spike 429 for each connector 407. The spike 429 is arranged to break through the septum 423 to establish fluid communication between the manifold 404 and the compartment 420. The spike 429 is removably located in the manifold 404 and is intended to be replaced when it has been worn down by successive septa penetrations.

The spike 429 has a central fluid channel 431 defined therein which connects to the central pipe 425 of the compartment 420 (Figure 17). A further fluid channel 433 is also defined in the spike 429 and, when the container 402 is fitted to the manifold 404, is in fluid communication with the interior of the compartment 420 via the diffuser 427. Thus, the

central fluid channel 431 and the central pipe 425 form a combined fluid channel which is concentric with the fluid channel formed by the neck of the connector 407. The type of spike 429 shown in Figure 15 is used to connect to the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 and also the first connector 407a of the glucose compartment 420 to form the fluid input channel 434 and the glucose output channel 436.

An alternative spike 429a is shown in Figure 18. In this form of spike 429a, the central fluid channel 431a connects the central pipe 425 of the compartment 418 directly to atmosphere so that the central pipe 425 acts as an air vent. This type of spike is used to connect the lactic acid compartment 408, the cleaning agent compartment 410, the calcium chloride compartment 416 and the magnesium chloride compartment 418 to the manifold 404 and also to connect to the second connector 407b of the glucose compartment 420, to form the glucose air vent channel 432.

As shown in Figure 18, the cap 406 includes a cover portion 435 which fits over the spike 429a when the cap 406 is in position over the manifold 404 for disinfection of the apparatus 100. The cover portion 435 redirects a flow of disinfection fluid which emerges from the further fluid channel 433 back into the central fluid channel 431a, so that the central fluid channel 431a is disinfected. If the cover portion 435 were not present, it would not be possible to direct disinfection fluid through the further fluid channel 433 into the central fluid channel 431a.

Figure 16 shows the manifold cap 406 removed from the manifold 404. To achieve this from the position shown in Figure 15, the container 402 is lifted by means of the container support rails 417 so that the cap 406 can pivot into the position shown in Figure 16. The cap 406 is attached to the manifold 404 by a spring-biased hinge 437 which ensures that the last part of the cap's movement onto the manifold 404 is linear, rather than rotational, so that there is no lateral abrasion of the seals between the manifold 404 and cap 406. A small D.C. motor (not shown) in the hinge 437 provides the

motive power to rotate the cap 406 into and out of position on the manifold 404. Alternatively, a spring mechanism may be used.

Figure 17 shows the container 402 in position on the manifold 404, with the septum 423 broken by the spike 429.

Figure 24 and Figure 25 show an alternative design of the compartments, for example compartment 408 or 418. Below, compartment 408 will be described. The design differs from the design described in connection with Figures 13 - 18 mainly in the arrangement of the air vent channel 424 and the fluid channel 426.

The neck portion of the compartment 408 comprises an insert 542 having a membrane 545 attached to its upper surface. The membrane 545 is for example an aluminium foil, which may be broken and penetrated by a spike 429. The central channel of the spike co-operates with the air vent channel 424 as in the previous designs.

Integral with the air vent channel 424 is arranged a first tube 544. The first tube may have a circular cross section but any shape is possible. Inside the first tube 544 is arranged a second tube 546 leaving a small space 548 to the first tube 544. At the bottom of first tube 544, the small space 548 opens to the interior of the compartment 408 in a narrow ring-shaped slit 550. The second tube 546 is at the top thereof provided with a hole 552 communicating the interior of the second tube with said small space 548. At the bottom thereof, the second tube 546 is connected to the ring-shaped channel of the spike 429 as shown.

In operation, in case of a compartment comprising powder which should be primed, water is entered via spike 429 into second tube 546 up to the top thereof. Water passes out through hole 552 to the small space 548 and flows down to the ring-shaped slit 550 from where it is directed sideways along the bottom surface of the compartment to prime and, if applicable, dissolve the powder in the compartment. The small space still maintain most of its air content, since water is passed slowly down along the exterior surface of the second tube 546 and along the interior surface of first tube 544.

After priming and when fluid is to be taken out from the compartment, a suction is exerted by the spike inside tube 546. Fluid is sucked via slit 550 and upwards in the small space 548 to opening 552. The air in the small slit is moved down the upper portion of the second tube 546 but maintain entrapped there. Fluid fills the rest of the second tube 546. Since the flow is slow in the second tube 546, the air stays in the upper portion.

If the compartment is disengaged from the spike, the fluid in the second tube 546 is given off to the manifold portion 404 (figure 5). The air cushion in the upper portion of the second tube 546 prevents further fluid to pass upwards in the small space 548, and no further fluid may pass out from the compartment. Thus, drips from the cartridge is prevented, apart from the first few drips at disengagement. In this design, the septum 423 used in the previously described design is no longer necessary.

Figure 25 shows the same compartment as if figure 24 with the spike in the engaged position.

This design may be used with the lactic acid compartment 408, which is in liquid form from the start. The same design may also be used for the other compartments enclosing powder components, inclusive the glucose compartment.

Returning to Figure 5, in normal operation of the concentrate mixing module 400, heated purified water from the thermal control and sterilisation module 300 enters the concentrate mixing module 400 through the mixing water feed connection 4a. A mixing system bypass valve 440 allows the purified water to be output through the mixing module output connection 4b without being processed by the concentrate mixing module 400, for example for sterilisation of downstream components. The water flow into the mixing system may be stopped by a mixing water stop valve 442.

Downstream of the mixing water stop valve 442 a glucose selector valve 444 is arranged to either allow the purified water to pass or to stop the flow of purified water and pass glucose solution from the glucose compartment 420 to the downstream components of the mixing system. In order to supply

water to the glucose compartment 420 for dissolving the glucose, the mixing system bypass valve 440 is opened and a reversible flow control pump 446 is used to draw purified water from the mixing water feed connection 4a and pump it through the glucose selector valve 444 to the glucose compartment 420 via the glucose input valve 490 and fluid input channel 434. The flow control pump 446 is a piston pump of similar construction to the Gambro standard part No. K1 4207 002 but having a 9 mm or 12 mm diameter, rather than the standard 6 mm diameter. A glucose recirculation pump 448, for example a gear pump or a centrifugal pump, recirculates the water through the glucose compartment 420 via the fluid input channel 434 and the glucose output channel 436, to ensure total dissolution of the glucose. During recirculation, the glucose input valve 490 is closed and the rest of the mixing module 400 can therefore operate independently while the glucose is being dissolved.

Downstream of the glucose selector valve 444 a mixing chamber 450 mixes the flow of purified water from the mixing water feed connection 4a (or glucose solution from the glucose compartment 420) with the flow from a reversible salt input displacement pump 452 (Gambro standard part K1 4207 002).

The flow control pump 446 is provided with a tachometer 454, and the salt input displacement pump 452 is also provided with a tachometer 456. The tachometers 454,456 monitor the volume flow rates of the respective pumps 446,452 in order to verify correct operation. When a pumping operation is carried out solely under control of the salt input displacement pump 452, the flow control pump 446 is bypassed by opening a flow control pump bypass valve 458. Both the salt input displacement pump 452 and the flow control pump 446 are piston pumps which have the necessary volumetric accuracy to control the salt concentration of the PD fluid. The maximum flow rate through the salt input displacement pump 452 is for example 50 ml/min and the maximum flow rate through the flow control pump 446 is for example 180 ml/min.

Downstream of the flow control pump 446, two independent mixing conductivity meters 460 monitor the composition of the salt solutions passing there through, in combination with

respective independent mixing temperature sensors 462. The two conductivity meters 460 and two temperature sensors 462 are provided for redundancy in the event of the failure of one meter or sensor. One of the meters and one of the temperature sensors communicates with the control system and the other meter and sensor communicate with the protective system, see Fig. 1a.

Downstream of the mixing conductivity meters 460 and the mixing temperature sensors 462, a drain disinfection valve 464 allows water from the mixing water feed connection 4a to be passed to the mixing module drain connection 15. The drain disinfection valve 464 is activated in this way during disinfection. In this case, the water entering the mixing water feed connection 4a has been heated to disinfection temperature by the thermal control and sterilisation module 300 and is then passed to the drainage module 500 via the drain disinfection valve 464 to disinfect the drainage module 500.

A reservoir filling valve 466 directs the fluid passing through the mixing conductivity meters 460 either to the mixing module output connection 4b or to a concentrate reservoir 468, which is used to store the concentrated PD fluid before it is diluted by a controlled flow of purified water. The concentrate reservoir 468 has a reservoir output valve 470 through which the concentrated PD fluid may be passed to the salt input displacement pump 452.

The concentrate reservoir 468 also has a reservoir air vent connection 472 which can be opened to atmosphere at the manifold cap 406 under the control of a reservoir air vent valve 496 to vent air during filling or emptying of the concentrate reservoir 468. Because the concentrate reservoir 468 contains concentrated PD fluid which will be supplied to the patient, the reservoir air vent connection 472 is disinfected. In order to achieve this and to disinfect the spikes 429, during disinfection, the manifold cap 406 is lowered onto the manifold 404 to form a sealed cavity as shown in Figure 15. This cavity can be filled with hot disinfecting fluid from the thermal control and sterilisation module 300 via the mixing water feed connection 4a, as described in detail

below. The air which is initially contained within the cavity formed by the manifold 404 and the cap 406 is passed to the drainage module 500 through the mixing module drain connection 15 via a cap air vent valve 474. Once all the air has been vented from this cavity, the cap air vent valve 474 provides a connection from the cavity formed by the manifold 404 and the manifold cap 406 to the mixing module drain connection 15 so that disinfection fluid can be circulated through the cavity. In this way, the reservoir air vent connection 472 can be completely disinfected, even though in operation of the system the reservoir air vent connection 472 is open to atmosphere. The reservoir air vent valve 496 is closed during this process, but can be opened once the manifold 404 and manifold cap 406 have been disinfected to pass disinfection fluid from the reservoir air vent connection 472 directly to the mixing module drain connection 15 to disinfect the reservoir air vent valve 496. The cavity formed by the manifold 404 and the manifold cap 406 is drained after disinfection by connecting the cavity to atmosphere at the manifold cap air vent 6 by opening the cap air vent valve 474. Disinfection fluid is then able to drain to the drainage module 500 via the reservoir vent disinfection valve 498, the reservoir air vent valve 496 and the mixing module drain connection 15.

The dissolution and mixing of the salts from the compartments of the disposable concentrate container 402 is effected by the opening and closing of the valves on the fluid lines 426,430 of the compartments 408-418, such that the salt input displacement pump 452 in a priming step can supply water to, and subsequently withdraw salt solution from, each of the compartments 408-418.

Each compartment 408-418 of the disposable concentrate container 402 is provided with a respective input valve, namely a lactic acid input valve 478, a cleaning agent input valve 480, a sodium bicarbonate input valve 482, a sodium chloride input valve 484, a calcium chloride input valve 486 and a magnesium chloride input valve 488. In addition, the function of the combined air vent and fluid channels 428 of the sodium bicarbonate compartment 412 and the sodium chloride compartment

414 is controlled by a sodium bicarbonate air vent valve 492 and a sodium chloride air vent valve 494, respectively.

The correct operation of these valves 478-488 is monitored using a salt input pressure sensor 476 in the following manner. After one of the input valves 478-488 has been operated and is closed, a signal is sent to all of the input valves 478-488 to close the valves. The salt input displacement pump 452 is then energised to pump water from the mixing water feed connection 4a towards the input valves 478-488. The pressure generated by the salt input displacement pump 452 is monitored by the salt input pressure sensor 476. In the event that one of the input valves 478-488 is stuck in the open position, a sufficiently high pressure will not be attainable and this fault condition will be detected by the salt input pressure sensor 476.

In the case of the first type of compartment 408,410,416,418 described above and taking the calcium chloride compartment 416 as an example, water from the mixing water feed connection 4a is drawn by the salt input displacement pump 452 through the mixing chamber 450 and is pumped through the calcium chloride input valve 486 into the calcium chloride compartment 416 via the fluid channel 426 of that compartment. All other input valves 478-488 of the other compartments 408-418 are closed. The air in the calcium chloride compartment 416 which is displaced by the water pumped into that compartment is vented to atmosphere through the air vent channel 424.

When the salt input displacement pump 452 has passed the required amount of water into the calcium chloride compartment 416, it is expected that all the calcium chloride powder that was in the compartment when the disposable concentrate container was loaded has been dissolved. The weight of calcium chloride in the calcium chloride compartment 416 is predetermined and the volume of water passed by the salt input displacement pump 452 is known, such that an approximation of the concentration of the calcium chloride solution formed in the calcium chloride compartment 416 can be derived.

The displacement pump 452 is driven by a step motor. Each step corresponds to a well defined volume of fluid pumped,

dependent on the rotational position of the step motor. The control system of the pump motor calculates the volume pumped by the pump in a accurate manner.

In order to transfer the necessary amount of calcium chloride solution to the concentrate reservoir 468, the flow control pump 446 is activated to draw water from the mixing water feed connection 4a at a predefined rate. The water is directed to the mixing module drain connection 15 by the drain disinfection valve 464. The salt input displacement pump 452 is activated to pump the calcium chloride solution at a controlled volume flow rate through the mixing chamber 450 via the flow control pump 446 through the mixing conductivity meters 460 to the mixing module drain connection 15. The flow rate through the mixing water feed connection 4a is reduced by an amount equal to the flow rate generated by the salt input displacement pump 452 because the flow rate through the flow control pump 446 is constant, whereby a predetermined dilution ratio is obtained. The mixing conductivity meters 460 measures the conductivity, and thus the concentration, of the diluted calcium chloride solution and the flow rate of the salt input displacement pump 452 is adjusted to achieve a predetermined concentration. Once the concentration is achieved, the drain disinfection valve 464 is switched and the reservoir filling valve 466 directs the calcium chloride solution to the concentrate reservoir 468, where it is stored until all the components of the concentrated PD fluid have been prepared. The total volume and the concentration of the calcium chloride solution which has passed through the flow control pump 446 into the concentrate reservoir 468 is therefore known and thus the amount of calcium chloride present in the concentrate reservoir. It is noted that the order of introduction of salts is closer described below.

A similar process to that for the dissolution and measurement of the calcium chloride solution is used for the preparation of the magnesium chloride solution from the magnesium chloride compartment 418. The cleaning agent is also dissolved in the cleaning agent compartment 410 in this way, when required. The lactic acid is routed to the concentrate

reservoir 468 without dilution. As explained below, the solution created with the cleaning agent is not a component of the PD fluid.

The solutions of sodium bicarbonate and sodium chloride are produced in a different manner to those for magnesium chloride and calcium chloride, because sodium bicarbonate and sodium chloride are used in greater amounts than magnesium chloride and calcium chloride. Taking as an example the preparation of sodium bicarbonate, all of the input valves 478-488 are closed, except for the sodium bicarbonate input valve 482. The sodium bicarbonate air vent valve 492 is set such that the combined air vent and fluid channel 428 of the sodium bicarbonate compartment 412 is connected to atmosphere via the manifold 404. The salt input displacement pump 452 pumps a measured quantity of water from the mixing water feed connection 4a via the mixing chamber 450 through the sodium bicarbonate input valve 482 and into the sodium bicarbonate compartment 412 via the combined priming and output channel 430. Sufficient water is introduced into the sodium bicarbonate compartment 412 that the sodium bicarbonate powder in the compartment 412 is fully immersed in water.

Once the sodium bicarbonate powder in the sodium bicarbonate compartment 412 is fully immersed the sodium bicarbonate air vent valve 492 is switched to provide a fluid path from the mixing water feed connection 4a to the combined air vent and fluid channel 428 of the sodium bicarbonate compartment 412. The salt input displacement pump 452 is reversed and draws a substantially saturated sodium bicarbonate solution out of the sodium bicarbonate compartment 412 through the combined priming and output channel 430 and the sodium bicarbonate input valve 482. The conductivity of the sodium bicarbonate solution is controlled and the solution is diluted and stored in the concentrate reservoir 468 in the same manner as for the calcium chloride solution described above.

The mixing and measuring of the sodium chloride solution is carried out in a corresponding manner.

The amounts of salt in each of the compartments 408-418 are chosen such that in correct operation each compartment 408-

418 produces a salt solution with a characteristic conductivity. Thus, if a malfunction of the system occurs whereby the wrong salt solution, for example magnesium chloride instead of calcium chloride, is produced, this will be identifiable from the conductivity measurement.

Furthermore, the salts are mixed at relatively high concentrations which provides an environment in which bacteria are unable to survive and thereby aids bacteriological control. The relatively high concentrations also allow the conductivity meters 460 to operate in a range in which measurement errors are relatively insignificant compared to the measured values, thereby increasing the accuracy of the concentration measurements.

The dissolution of the glucose solution has been described above. A required amount of the glucose solution is pumped to the concentrate reservoir 468 via the glucose input valve 490, glucose selector valve 444 and the reservoir filling valve 466 by the flow control pump 446. This pump is used because it has a high capacity, whereby the metering of the glucose may take place in a shorter time.

At the end of the dissolution and measuring operation, the concentrate reservoir 468 contains concentrated PD fluid with the correct relative proportions of salts and glucose required by the patient's individual prescription but at a higher absolute concentration. Thus, it is then only necessary to add water to this concentrated PD fluid to obtain PD fluid according to the patient's prescription.

When it is desired to provide the PD fluid to the patient through the mixing module output connection 4b, a measured flow (around 50 ml/min) of concentrated PD fluid is drawn from the concentrate reservoir 468 via the reservoir output valve 470 by the salt input displacement pump 452, which pumps the concentrated PD fluid into the mixing chamber 450. The flow control pump 446 is bypassed by opening a flow control pump bypass valve 458 and a constant flow (around 300 ml/min) of PD fluid is drawn out of the mixing module output connection 4b by the volumetric pump 352 of the thermal control and sterilisation module 300, see figure 4. The flow out of the

mixing module output connection 4b is greater than that produced by the salt input displacement pump 452, and the additional fluid flow (around 250 ml/min) that is not provided by the salt input displacement pump 452 is drawn from the mixing water feed connection 4a. In this way, the concentrated PD fluid from the concentrate reservoir 468 is diluted in the mixing chamber 450 with water from the mixing water feed connection 4a so that PD fluid at the desired concentration exits the concentrate mixing module 400 via the mixing module output connection 4b. The concentration of the PD fluid is monitored by the mixing conductivity meters 460 and is controlled by varying the flow rate through the salt input displacement pump 452.

The dilution of the concentrated PD fluid from the concentrate reservoir 468 in this way not only reduces the salt and glucose concentration of the PD fluid to the required level, but also ensures that the level of dissolved gas in the PD fluid is low and below the medically required maximum level. The inventors have assumed that by the time the concentrated PD fluid in the concentrate reservoir 468 is ready for use it will be, at most, saturated with dissolved gas which has entered the system during dissolution of the salts and glucose. However, the water entering the concentrate mixing module 400 at the mixing water feed connection 4a has been degassed by the water preparation module 200. The dilution ratio of the flows of the concentrated dialysis fluid pumped by the salt input displacement pump 452 and the water entering the mixing water feed connection 4a has been chosen to be at least sufficient to dilute the gas-saturated concentrated dialysis fluid to a dissolved gas content below the medically required level.

The flow through the RO membrane disinfection connection 3 is controlled by an RO membrane disinfection valve 499. During disinfection, water at disinfection temperature is supplied to the mixing water feed connection 4a by the thermal control and sterilisation module 300 and is pumped by the salt input displacement pump 452 through the mixing water stop valve 442, the glucose selector valve 444, the mixing chamber 450 and the RO membrane disinfection valve 499 via the RO membrane

disinfection connection 3 to the water preparation module 200.

After the concentrate disposable container 402 is put in place and into engagement with the spikes 429 in the manifold 404, the following sequence of operations takes place.

First, the cleaning agent compartment 410 is primed with water by the introduction of 80 ml of water into the cleaning agent compartment 410, which comprises 20 g sodium carbonate, in order to thereby produce a sodium carbonate solution having a concentration of about 2284 mmol/l. The sodium carbonate solution is used for cleaning purpose as described above.

The peritoneal dialysis fluid is composed from six separate substances namely magnesium chloride, calcium chloride, sodium bicarbonate, sodium chloride, lactic acid and glucose. The amount of material in each compartment 410-420 is given in Table 2.

In order to prime the disposable concentrate container 402, firstly 962 ml of water is introduced into the glucose compartment 420 by the flow control pump 446. Since the flow control pump 446 can operate at about 180 ml/min, this introduction will take approximately 5.5 minutes. Then the glucose input valve 490 is closed and the glucose recirculation pump 448 is operated in order to recirculate the glucose in the glucose compartment 420 to promote full dissolution.

Thereafter, the magnesium chloride input valve 488 is opened to introduce 48.4 ml of water into the magnesium chloride compartment 418. Then the magnesium chloride input valve 488 is closed and the calcium chloride input valve 486 is opened to introduce 145.2 ml of water into the calcium chloride compartment 416. These introductions of water are performed by the salt input displacement pump 452, which has a maximum capacity of about 50 ml/min. The above two priming steps will take about 4 minutes together. The magnesium chloride and the calcium chloride are fully dissolved in the water introduced, either during the introduction of water into the compartment or shortly thereafter to finally dissolve all of the salt particles.

Then the water is introduced into the sodium bicarbonate compartment 412 by opening the sodium bicarbonate input valve

482 and introducing about 60 ml of water by means of the salt input displacement pump 452. The exact amount of water introduced into the sodium bicarbonate compartment 412 is not crucial provided the water level does not rise above the combined air vent and fluid channel 428 so that water is not passed down that channel 428 to the manifold 404 via the sodium bicarbonate air vent valve 492. If a small portion of the water nevertheless does pass this way, this is of no consequence.

The same procedure is performed for the sodium chloride compartment 414 by the introduction of approximately 100 ml of water into the compartment by means of the salt input displacement pump 452. All of the powder in the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 is not completely dissolved, because the water quantity is insufficient to dissolve all of the powder.

No water is added to the lactic acid compartment 408, which comprises 120 g lactic acid having a concentration of 30%.

By means of the above described priming procedure, the different compartments 408-420 will comprise electrolyte solutions of the salts and glucose having the following concentrations when taken out from the respective compartments at 25°C:

magnesium chloride	2455.8 mmol/l
calcium chloride	2117.3 mmol/l
sodium bicarbonate	1199 mmol/l
sodium chloride	5253 mmol/l
lactic acid	3500 mmol/l
glucose	3393.6 mmol/l

The exact order of priming of the compartments may differ from the order given above.

The next step in the procedure is to transfer measured amounts of the electrolytes and the glucose to the concentrate reservoir 468. The resulting solution in the concentrate reservoir 468 may be a solution having five times the concentration of the final required solution. The concentrate

reservoir solution is then diluted by 1:5 before being sent to the OLA 375 for sterilisation before introduction into the peritoneal cavity of the patient. Thus, the concentrate reservoir 468 should comprise 600 ml of concentrated solution in order to provide 3000 ml of final peritoneal dialysis solution after dilution.

The first substance to be introduced into the concentrate reservoir 468 is sodium bicarbonate. The sodium bicarbonate air vent valve 492 is adjusted to connect the combined air vent and fluid channel 428 with the mixing water feed connection 4a and the sodium bicarbonate input valve 482 is opened to connect the combined priming and output channel 430 with the salt input displacement pump 452. By operating the salt input displacement pump 452, substantially saturated sodium bicarbonate solution is taken out from the bottom of the sodium bicarbonate compartment 412 and water from the water preparation module 200 is introduced into the top of the sodium bicarbonate compartment 412 via the combined air vent and fluid channel 428. In order to provide a bicarbonate concentration of 40 mmol/l in the final solution, it is required to transfer 120 mmol of sodium bicarbonate to the concentrate reservoir 468, which corresponds to 100 ml pumped by the salt input displacement pump 452. Thus, the salt input displacement pump 452 may be operated at a pump speed of 40 ml/min in 2.5 minutes in order to provide the required amount. At the same time the flow control pump 446 is adjusted to 60 ml/min in order obtain a dilution ratio of 1:1.5 resulting in a conductivity of approximately 35 mS/cm.

As described before, the mixed solution is passed to the drainage module 500 via the drain disinfection valve 464 and the mixing module drain connection 15 until a stable value has been obtained from the mixing conductivity meters 460. Then the drain disinfection valve 464 and the reservoir filling valve 466 are switched over in order to transfer the solution to the concentrate reservoir 466.

The conductivity measurement at the mixing conductivity meters 460 is converted to the corresponding concentration of sodium bicarbonate by the control system and is multiplied by

the flow velocity as measured by tachometer 454 of the flow control pump 446 to thereby obtain the amount of sodium bicarbonate per minute passing through the mixing conductivity meters 460. By integrating this amount per minute over time, the total amount of material delivered to the concentrate reservoir 468 is obtained. When 120 mmol have been transferred, the reservoir filling valve 464 is switched over in order to stop further introduction into the concentrate reservoir 468 and direct the solution to the drainage module 500 via the mixing module drain connection 15. The fact that the correct amount of material has been delivered to the concentrate reservoir 468 can also be controlled by the tachometer 456 of the salt input displacement pump 452, which should pump 100 ml.

Immediately after the shifting over of the reservoir filling valve 464, the salt input displacement pump 452 is reversed to pump clean water in the opposite direction to push back the sodium bicarbonate present in the tubes between the sodium bicarbonate input valve 482 and the mixing chamber 450, in order to save material and also in order to flush the tube system with clean water. The volume of substantially saturated sodium bicarbonate so recovered is relative small, but may still be significant. A corresponding volume of air is transferred into combined air vent and fluid channel 428 since there is normally an air cushion at the top of compartment 412. During the next operation of the compartment, this air volume is reintroduced into compartment 412.

The flow control pump 446 operates to flush the rest of the pipe system downstream of the mixing chamber 450 of any sodium bicarbonate.

If the peritoneal dialysis fluid is to comprise substantially only bicarbonate as buffer, the final concentration of the buffer can be adjusted by the adjustment of the amount of bicarbonate introduced into the concentrate reservoir 468. Introduction of 100 ml will result in a final bicarbonate concentration of 40 mmol/l and introduction of 87.5 ml will result in a final bicarbonate concentration of 35 mmol/l. The pH may be adjusted by the addition of lactic acid.

If the final peritoneal dialysis fluid is to comprise a

mixture of sodium bicarbonate and sodium lactate, for example 25 mmol/l bicarbonate and 15 mmol/l sodium lactate, the following procedure is followed. Any mixture from about 5:35 to 35:5 can be obtained or any other total sum than 40.

The lactic acid input valve 478 is opened to connect the lactic acid compartment 408 with the salt input displacement pump 452. The mixing water stop valve 442 is closed to prevent dilution of the lactic acid and the flow control pump bypass valve 458 is opened to bypass the flow control pump 446. If 15 mmol/l of sodium lactate is desired, the salt input displacement pump 452 pumps 16 ml of lactic acid (30% concentration) into the concentrate reservoir 468. The concentration of the lactic acid solution may be monitored by the mixing conductivity meters 460, which should show a conductivity value of approximately 39 mS/cm.

During the introduction of lactic acid into the bicarbonate solution in the concentrate reservoir 468, the acid reacts with the bicarbonate ions and forms carbon dioxide, which is vented to atmosphere via the reservoir air vent connection 472, the reservoir air vent valve 496 and the cap air vent valve 474. At the top of the concentrate reservoir 468, a cushion of carbon dioxide is formed, which is not transferred to the surrounding atmosphere. Thus, the carbon dioxide partial pressure will be one atmosphere (1 Bar) which results in a dissolved carbon dioxide concentration of about 23 mmol/l at equilibrium in the liquid in the concentrate reservoir. The formation of carbon dioxide is comparatively fast, but a short pause may be required until the carbon dioxide generation has ceased.

Once again the salt input displacement pump 452 is reversed for pushing back the lactic acid into the lactic acid compartment 408 until water reaches the lactic acid input valve 478 or shortly there before, and the tube system is flushed with water via the flow control pump 446.

Next, sodium chloride is introduced into the concentrate reservoir 468. In order to provide 140 mmol/l in the final solution, 470 mmol has to be transferred to the concentrate reservoir 468, which corresponds to 80 ml of concentrated

solution. Since sodium chloride has a very high conductivity, the sodium chloride is diluted as much as possible in the mixing chamber 450. However, the dilution can not be too large because of restrictions in the final volume in the concentrate reservoir 468. As an example a dilution ratio of 1:4 is given below. Thus, the flow control pump 446 is adjusted to 40 ml/minute and the salt input displacement pump 452 is adjusted to 160 ml/min resulting in a conductivity of about 98 mS/cm. The same integration method as described above for sodium bicarbonate is used in order to determine when a sufficient amount of sodium chloride has been introduced into the concentrate reservoir 468. Alternatively, it is determined when the salt input displacement pump 452 has pumped 80 ml, which should be approximately after two minutes.

Again the salt input displacement pump 452 is reversed to push back the sodium chloride solution into the sodium chloride compartment 414 and some air into combined air vent and fluid channel 428.

Then, the glucose input valve 490 is opened to transfer glucose to the concentrate reservoir 468. If 1.5% final glucose concentration is to be obtained, 75 ml glucose solution should be transferred, if 2.5% is to be obtained, 125 ml should be transferred, and if 4.0% is to be obtained, 200 ml should be transferred. In order to save time, the flow control pump 446 is used for this purpose. Glucose has no inherent conductivity, which is checked by the mixing conductivity meters 460. When the correct amount has been introduced as measured by tachometer 454, the glucose selector valve 444 is operated to transfer water from the mixing water feed connection 4a via the flow control pump 446 to flush the tube system. The flow control pump 446 may first be reversed while the mixing system bypass valve 440 is opened to push back glucose to the glucose compartment 420 as described above, if desired. Since the recovered volume is small compared to the volume in the glucose department, the recovery may not be used for glucose.

The dilution ratio of sodium chloride is selected in dependence on the desired glucose concentration so that the volume obtained in the concentrate reservoir 468 so far is

approximately 570 ml.

Finally, magnesium and calcium are introduced into the concentrate reservoir 468. These substances are introduced as late as possible when the bicarbonate is diluted to a low concentration to avoid problems with precipitation.

First magnesium chloride is introduced by opening the magnesium chloride input valve 488 and operating the salt input displacement pump 452. Only 1.5 mmol magnesium chloride should be transferred by the salt input displacement pump 452, which corresponds to 0.6 ml, to obtain a final concentration of 0.5 mmol/l. The salt input displacement pump 452 is able to meter such small quantities with sufficient accuracy. The pump has a displacement of 228 microlitre per revolution and is controlled over 1/100 revolution.

Magnesium chloride is not introduced in concentrated form into the concentrate reservoir 468 to avoid local precipitation. Thus, the flow control pump 446 is operated with 10 times the speed of the salt input displacement pump 452 to obtain a dilution ratio of 1:10. Then the conductivity of the magnesium chloride solution will be around 35 mS/cm. By integrating the concentration obtained from the mixing conductivity meters 460 multiplied with the flow velocity obtained from the flow control pump 446, the delivered amount is obtained. The delivered amount is checked by the salt input displacement pump 452, which should pump 0.6 ml. After completion of the introduction into the concentrate reservoir 468, the salt input displacement pump 452 is reversed to push back magnesium chloride into the magnesium chloride compartment 418. This procedure is of importance for magnesium chloride and calcium chloride, which are provided in small quantities.

Finally, the same procedure is performed for calcium chloride. In order to provide 1.5 mmol/l calcium in the final solution, it is necessary to transfer 4.5 mmol corresponding to 2.1 ml concentrated solution to the concentrate reservoir 468. As for magnesium, this process is performed by dilution in the ratio of 1:10. The conductivity will then be approximately 34 mS/cm.

When calcium ions are mixed with bicarbonate ions, there

is always a risk of calcium carbonate precipitation. By keeping an air cushion comprising carbon dioxide above the surface of the concentrate reservoir 468 and thereby providing a saturated carbon dioxide gas content in the solution, it is assured that the pH of the solution is as low as possible, whereby no precipitation will take place.

To assure the highest possible content of carbon dioxide before mixture with calcium chloride, lactic acid may be introduced as late as possible in the mixing procedure, i.e. immediately before the addition of magnesium chloride and calcium chloride, to obtain carbon dioxide generation and saturation of the complete solution with carbon dioxide. The order of sodium bicarbonate, sodium chloride and glucose may also be different from that given above, for example first sodium chloride, then glucose and then sodium bicarbonate.

After the formation of the concentrated PD solution in the concentrate reservoir 468, it is diluted in the ratio of 1:5. In this mode of operation, the OLA pump 352 is operated at 300 ml/min and the salt input displacement pump 452 is operated at 60 ml/min to obtain a dilution ratio of 1:5. The mixing conductivity meters 460 control the concentration of the mixed solution and adjust the salt input displacement pump 452 to avoid variation in the conductivity.

A slightly modified mixing portion is disclosed in Figure 5a. A metering pump 448a is inserted in the pipe between the glucose input valve 490 and the glucose selector valve 444. The metering pump 446a is shunted by a valve 490a. The glucose selector valve 444 is replaced by a direct connection to the mixing chamber 450. These additional components enable the measurement of the glucose concentration in the glucose compartment 420. The operation is as follows.

After dissolution of the glucose in the water introduced into the glucose compartment 420, the glucose should have a concentration of 50%. However, there is always a risk of errors and there is a desire to be able to control the glucose concentration.

To start this glucose check procedure, the sodium chloride input valve 484 and the sodium chloride air vent valve

494 are opened, the salt input displacement pump 452 is operated and the flow control pump 446 is operated in order to provide a sodium chloride solution having a concentration of about 500 mmol/l, i.e. a dissolution ratio of about 1:10. The mixing conductivity meters 460 should measure approximately 46.7 mS/cm. The flow control pump 446 is operated at approximately 50 ml/min and the salt input displacement pump 452 at approximately 5 ml/min. Then the glucose input valve 490 is opened and the metering pump 448a is operated to pump glucose solution from the glucose compartment 420 via the fluid input channel 434, the glucose input valve 490 and the metering pump 448a into the mixing chamber 450. The metering pump 448a is driven at for example 20 ml/min.

The introduction of glucose into the sodium chloride solution in the mixing chamber 450 results in a decrease of the conductivity as measured by the mixing conductivity meters 460. The decrease is substantially proportional to the concentration of the glucose solution. Thus, the glucose concentration in the glucose compartment 420 can be monitored.

After measuring the glucose concentration, the above described procedure may take place.

Alternatively, the mixture obtained as described in relation to Figure 5a, i.e. a mixture of glucose and sodium chloride, may be transferred to the concentrate reservoir 468. In that case, the sodium salt input displacement 452 should have a higher speed to ensure that the amount of water introduced into the concentrate reservoir 468 is not too high.

It is possible to obtain the same operation by using the glucose recirculation pump 448 as a reversible metering pump instead of a separate metering pump 448a.

It would also be possible to use the lactic acid and dilute it with glucose to monitor the lowering of conductivity. In that case, no additional pump is required compared to Fig. 5. The operation would be to open the lactic acid input valve 478, adjust the salt input displacement pump 452 to 10 ml/min, adjust the flow control pump 446 to 15 ml/min, with the glucose selector valve 444 and the mixing water stop valve 442 open to permit 5 ml/min of water to pass into the mixing chamber 450

from the mixing water feed connection 4a. The conductivity is measured. Then, the glucose input valve 490 is opened and the glucose selector valve 444 is switched over to replace the water supply (5 ml/min) to the mixing chamber 450 with glucose. The decrease in conductivity is monitored and a calculation is made to determine the corresponding concentration of glucose.

In Figure 5a there is shown an electric heater 438a in the fluid input channel 434 to glucose compartment 420 to heat the recirculated glucose solution during the dissolution process to promote dissolution. Glucose becomes cooler during dissolution and therefor needs heating to maintain a temperature of for example 40°C during the complete dissolution step.

Another alternative design of the glucose metering step is shown on Fig. 5b and Fig 4a. Turning first to Fig. 5b, the metering pump 448a has been replaced by a reversible metering pump 448b. Metering pump 448b is constructed to be able to pump the glucose solution against a back pressure of several bar, more than 3 bar and preferably more than 6 bar or reasons appearing below. A valve 490a bypasses the pump 448b. A glucose input valve 490b is arranged between mixing chamber 450 and inlet tube 434 to prime the glucose in compartment 420.

The operation of the alternative arrangement according to Fig. 5b is the same as described above in connection with Fig. 5 or Fig. 5a, except that the glucose is not entered in concentrate reservoir 468. Instead, the concentrated glucose is metered by metering pump 448b and transferred via the activated valve 490b to an outlet connection 4c, leading to an input connection in the middle of the OLA steriliser, as indicated on Fig. 4a.

In the alternative OLA steriliser arrangement shown of Fig. 4a, the oil bath arrangement 364 - 368 is replaced by an electric heater 364a. The inlet fluid entering the OLA arrangement via inlet 4b, valve 356 and heat exchangers 360 and 362 is an electrolyte fluid having components which are not sensitive to heat. Thus, the electrolyte fluid may be heated with an electric heater without risk of decomposition or the formation of harmful substances, although an electric heater

may have spots of high temperature. The heat sensitive portion of the final solution, namely the glucose is entered after the electric heater 364a at inlet 4c. At this position, the electrolyte fluid is at a high temperature of for example 150°C and at a high pressure of for example 6 bar absolute pressure. The inlet fluid heats the concentrated glucose solution rapidly to a high temperature of for example 148°C. The combined fluid is maintained at a high temperature for a predetermined time period determined by the flow distance in a coil 363. Then, the combined fluid is cooled rapidly in heat exchangers 362 and 360. The temperature is monitored by temperature sensors 370. By this operation, the sensitive glucose portion is heated in a substantially square temperature curve, which is beneficial for the sterilisation and for avoiding the formation of glucose degradation products. The sterilisation of the glucose portion may be very well controlled in order not to over-sterilise the glucose. The fact that the electrolyte fluid may become slightly over-sterilised means no disadvantage.

It is possible to include calcium and magnesium ions in the glucose fluid to be late introduced in the OLA arrangement of Fig. 4a in order to avoid possible problems with calcium carbonate precipitation and scaling of the tube portions in the mixing arrangement of Fig. 5b. In this embodiment, calcium chloride and magnesium chloride is transferred to the glucose compartment 420 after the dissolution of the glucose but before the metering of the glucose to output connection 4b. Valve 486 is opened and pump 452 is operated to withdraw calcium chloride from compartment 424. Valve 442 and valve 458 are closed and pump 446 is inoperative. Valve 490 b is placed in the position shown on Fig. 5b and valve 490a is opened. The calcium chloride fluid metered by pump 452 must pass via mixing chamber 450 and valves 490b and 490a to the glucose compartment 420. The amount of calcium chloride transferred to glucose compartment 420 is carefully monitored by the metering pump 452. The same operation takes place for magnesium chloride.

Finally, the combined glucose, calcium chloride and magnesium chloride is metered to output 4c to be included in the final PD fluid. By this arrangement, sodium bicarbonate and

calcium chloride are not mixed until in the diluted PD fluid, which means that the risk of precipitation is minimised.

Alternatively, the calcium chloride may be metered by metering pump 452 to mixing chamber 450. Flow control pump 446 is operated to dilute the calcium chloride and the fluid is measured in conductivity meters 460. The measured and diluted calcium chloride is then transferred to glucose chamber via a valve 464a shown in broken lines in Fig. 5b. The same operation takes place with magnesium chloride.

Alternatively, or in combination, (part of) calcium chloride and/or magnesium chloride may be transferred to concentrate reservoir 468 as previously described.

Drainage Module 500

The drainage module 500 is shown in detail in Figure 6. The fluid supplied to the drainage module 500 by the ambient pressure drain connection 14b and the mixing module drain connection 15 is routed directly to the heat recovery drain connection 13b from which it passes to the thermal control and sterilisation module 300 for heat recovery before being returned to the heat recovery drain return connection 13c. The fluid entering the heat recovery drain return connection 13c passes to the external waste connection 16 via a heat recovery return valve 532. The temperature of the fluid exiting the heat recovery drain connection 13b is monitored by a drain disinfection temperature sensor 530.

Water from the thermal drain connection 13a, which originates from the purification waste connection 2d of the water preparation module 200, passes through a thermal drain connection valve 520 directly to the external drain connection 16.

Fluid from the negative pressure drain connection 14a passes through a pressure conditioning chamber 510 under a negative pressure generated by a drainage pump 508 and then passes to the heat recovery drain connection 13b via the drain disinfection temperature sensor 530. The pressure conditioning chamber 510 is in the form of a chamber closed by a movable, spring-biased diaphragm, and is provided to prevent pressure

fluctuations due to the drainage pump 508 from being passed to the patient along the negative pressure drain connection 14a, and also to make control of the draining process easier. The drainage pump may be a peristaltic pump or gear pump, or a pump generating a predetermined maximum pressure, like a centrifugal pump.

The conditioning chamber 510 moreover ensures that the patient is not exposed to large negative pressures. For this purpose, the conditioning chamber 510 may be provided with limit switches 512 and 514 that monitors the position of a spring loaded piston 516 in the chamber 510. The switches may be used for controlling the drainage pump 508 to provide a negative pressure compatible with safe patient conditions during drainage of the patient, such as not exceeding 1 meter of water pillar negative pressure in relation to the atmosphere.

For disinfection, hot disinfecting fluid enters the drainage module 500 through the mixing module drain connection 15, the negative pressure drain connection 14a and the ambient pressure drain connection 14b. The disinfecting fluid is passed from the drainage module 500 along the heat recovery drain connection 13b to the thermal control and sterilisation module 300 via the drain disinfection temperature sensor 530. The heat from the disinfection fluid is recovered in the thermal control and sterilisation module 300 and the fluid is returned to the drainage module 500 via the heat recovery drain return connection 13c which passes the fluid to the external waste connection 16 via the heat recovery return valve 532. Chemical disinfectant (or hot water in the case of heat disinfection) from the water preparation module 200 enters the drainage module 500 through the thermal drain connection 13a and passes directly to the external drain connection 16.

Cycler and sterilisable connector module 600

The cycler and sterilisable connector module 600 is shown in detail in Figure 7. In normal operation, sterile PD fluid is provided to the cycler and sterilisable connector module 600 via the sterile fluid connection 8a and passes through a

patient fill valve 602 to a dialysate line sterilisable connector 604. The sterilisable connector 604 may be of the type described in International patent application WO96/05883 (Gambro AB) which is incorporated herein by reference.

The operation of the sterilisable connector 604 is shown schematically in Figures 19a to 19d. Referring to Figure 19a, the sterilisable connector 604 is arranged to receive a double male connector 630 at the end of the disposable fluid line 10 in two corresponding chambers 632. The end of each prong of the male connector 630 is closed by a pierceable membrane 634. The membranes 634 are pierced by respective membrane spikes 636 when the male connector 630 is fully inserted in the chambers 632, as shown in Figure 19c. The membrane spikes 636 have channels defined there through for fluid flow in the direction of the arrows in Figures 19b and 19c. The chambers 632 are connected by a fluid passage 638 which can be opened or closed by a connector valve 640. In an alternative embodiment, there is no connector valve 640, as shown in Fig. 19b.

Initially, the male connector 630 is partially inserted into the chambers 632 as shown in Figure 19b. The connector valve 640 is opened and water at sterilisation temperature and pressure (3 bar) is circulated through the membrane spikes 636, the chambers 632 and the fluid passage 638 in the direction of the arrows in Figure 19b. The circulation of the sterilising water sterilises the chambers 632, the membranes 634 and the membrane spikes 636. Once this sterilisation operation has been completed, the male connector 630 is inserted all the way into the chambers 632, so that the membranes 634 are pierced and a fluid path is opened through the membrane spikes and into the disposable dialysate line 10. At the same time, the fluid connection between the chamber 632 and the fluid passage 638, as well as an area around the spikes, is closed off by the male connector 630. Fluid, for example PD fluid, can then flow in the direction of the arrows shown in Figure 19c during a rinsing step or for filling and draining a peritoneal cavity of a patient.

At the end of the treatment session, the flow of PD fluid into the sterilisable connector 604 is stopped, the connector

valve 640 is closed and the male connector 630 is partially withdrawn from the chambers 632 so that air can enter the disposable fluid line 10 through a recess 642 formed in the wall of the inlet chambers 632. The remaining fluid in the disposable fluid line 10 can then be pumped out to drain the disposable dialysate line 10, as indicated by the arrows in Figure 19d.

Referring back to Figure 7, from the sterilisable connector 604, the PD fluid passes out of the patient fill connection 9a through the disposable fluid line 10 to the patient's peritoneal cavity. Patient pinch valves 624, which open and close together, are provided on the patient fill connection 9a and the patient drain connection 9b to allow the machine to physically stop the flow of PD fluid in an emergency by pinching the disposable fluid line 10 between two jaws (not shown) which are normally closed. The pinch valves 624 are only opened by the control system and the protective system if it is sure that the apparatus is operating correctly and it is safe to deliver PD fluid to the patient.

The pinch valves are also opened during insertion of the disposable line set before use.

Figure 20 shows the disposable fluid line 10 for connection to the sterilisable connector 604. From the male connector 630, two separate tubes 644 extend to a Y-connector 646. The Y-connector 646 connects the two pipes 644 to a standard catheter connector 654 via a manual pinch valve 648. The catheter connector 654 is the only patient connection in the whole apparatus 100 which is not machine sterilised. In contrast, traditional PD treatment systems include several aseptic connections which may introduce potentially harmful bacteria into the peritoneal cavity and lead to peritonitis. Because the apparatus includes only one aseptic connection, the risk of peritonitis is significantly reduced. The only aseptic connection may be replaced by a sterile connection, for example a connection performed by a sterile welding device, cutting a portion of the end of the line set 10 and a portion of a patient tube with a hot wafer and immediately joining the hot ends to obtain a sterile connection. The patient tube is

partially consumed and need to be replaced with certain intervals. This technique is well known and used. Another connection technique claimed to be sterile is a connector sterilised by ultraviolet light during the connection cycle.

The distance between the Y-connector 646 and the catheter connector 654 is kept as small as possible so that the dead space in the disposable fluid line 10 is small, such as less than 2 ml. The pressure drop in one direction across the disposable fluid line 10 is small, such as less than 40 mbar (4 kPa) at a flow rate of 300 ml/min.

Figure 21 shows an alternative version of the disposable dialysate line 10a, which is used when a sample of the patient's dialysate is to be collected. The sampling disposable dialysate line 10a comprises, in addition to the features of the normal disposable dialysate line 10, a syringe 652 which fits into a drive mechanism (not shown) in the sampling module 700. The syringe 652 draws off 15 ml of the drained dialysate. Since the dialysate is mixed within the body, the sampling may take place any time during the drain cycle and will represents an average of the whole treatment session. The filled syringe 652 can then be broken off from the sampling disposable dialysate line 10a by means of a self-sealing frangible connection (not shown) and sent for analysis. If desired, the syringe can be visually examined to check the clarity of the dialysate.

Referring back to Figure 7, when it is desired to empty the patient's peritoneal cavity, the drained fluid is drawn through the disposable fluid line 10 to the patient drain connection 9b, through the sterilisable connector 604, and then through a patient drain cut-off valve 606. From the patient drain cut-off valve 606 the drained fluid passes through a first patient drain valve 608 and past two independent patient drain pressure sensors 610, which monitor that the negative pressure applied to the peritoneal cavity of the patient by the negative pressure drain connection 14a is not so great as to harm the patient. Downstream of the patient drain pressure sensors 610 the output volumetric flow meter 650 measures the volume of fluid removed from the patient's peritoneal cavity,

and a second patient drain valve 612 is provided downstream of the volumetric flow meter 650 to close off the negative pressure drain connection 14a.

A sterilisation bypass valve 614 allows a fluid path to be opened from the sterile fluid connection 8a to the negative pressure drain connection 14a without going through the patient, when a patient bypass valve 616 is open. The PD fluid can be directed directly to the ambient pressure drain connection 14b, without passing through the patient, by opening a sterilisation heat recovery bypass valve 618 downstream of the patient bypass valve 616.

During filling of the patient, the pressure of the PD fluid entering the peritoneal cavity is monitored by closing the patient bypass valve 616, the sterilisation bypass valve 614 and the second patient drain valve 612, and opening the first patient drain valve 608 and the patient drain cut-off valve 606. In this way the pressure at the patient's peritoneal cavity is transmitted back from the Y-connector 646 of the disposable fluid line 10 via the patient pinch valve 624, the patient drain cut-off valve 606 and the first patient drain valve 608 to the patient drain pressure sensors 610, although there is no flow along this fluid path because the second patient drain valve 612 is closed. By means of this arrangement, the patient drain pressure sensors 610 can measure accurately the pressure of the fluid entering the patient's peritoneal cavity during filling thereof, because the pressure measurement is made as close to the peritoneal cavity as possible.

The pressure sensors 610 may control the drain pump 508 to start operation (and opening of valve 612) if the positive pressure becomes too large, such as more than 2 meter water pillar over atmosphere pressure, to thereby shunt a portion of the fill fluid to the waste.

A pressure conditioning chamber 660 similar to pressure conditioning chamber 510 may be provided after patient fill valve 602 as shown by broken lines in Fig 7. The operation of chamber 660 is the same as described for chamber 510.

Alternatively, the patient drain cut-off valve 606 can be

closed and the patient bypass valve 616 and the sterilisation bypass valve 614 can be opened, with the sterilisation heat recovery bypass valve 618 closed. In this way, a pressure tap from the sterile fluid connection 8a to the patient drain pressure sensors 610 is formed, such that the patient drain pressure sensors 610 can measure the pressure of the fluid entering the peritoneal cavity of the patient along the sterile fluid connection 8a.

Monitoring of the pressure at the peritoneal cavity, enables the control system to detect whether the patient has blocked or disconnected the disposable dialysate line 10.

During sterilisation of the sterilisable connector 604, hot sterilising fluid enters the cycler and sterilisable connector module 600 under pressure through the sterile fluid connection 8a and passes through the patient fluid valve 602, through the sterilisable connector 604, through the patient drain cut-off valve 606, and through the sterilisation bypass valve 614 to the sterilisation output connection 8b. The first patient drain valve 608 is closed during sterilisation to prevent the sterilising fluid reaching the output volumetric flowmeter 650, which may be damaged at the sterilisation temperature, and also to prevent the patient drain pressure sensors 610 from being subjected to the high pressure required to stop the water at sterilisation temperature from boiling. Flow meters and pressure sensors that have the necessary accuracy for this role and can withstand the sterilisation pressure and temperature are expensive. Thus, the provision of the first patient drain valve 608 reduces the cost of the apparatus 100.

The heat from the sterilising fluid is recovered in the thermal control and sterilisation module 300 and the cooled fluid is returned to the cycler and sterilisable connector module 600 through the sterilisation fluid return connection 8c. The fluid passes to the ambient pressure drain connection 14b through a sterilisation pressure release valve 620 to return the fluid to ambient pressure and through a sterilisation return shut-off valve 622.

In a second sterilisation route, the patient fill valve

602 is closed and the patient bypass valve 616 is opened so that sterilisation fluid at high temperature and pressure can pass from the sterile fluid connection 8a to the sterilisation output connection 8b via the patient bypass valve 616.

For disinfection, fluid at disinfection temperature is passed through the fluid lines of the cycler and sterilisable connector module 600 and out through the negative pressure drain connection 14a and the ambient pressure drain connection 14b, to disinfect those components which are not sterilised.

Operation of the apparatus

The operation of the apparatus 100 as a whole will now be described. The default state of all valves is closed for most of the valves. Thus, in its initial operating mode, the inlet valve 202 of the water preparation module 200 and the thermal drain connection valve 520 and the heat recovery return valve 532 of the drainage module 500 are closed, as are the patient pinch valves 624 of the cycler and sterilisable connector module 600. In this state therefore the apparatus is sealed off from the external environment.

Initially, the concentrate disposable container 402 is not connected to the manifold 404, but the disposable fluid line 10 (with membranes 634 intact) is partially inserted in the sterilisable connector 604. All of the pumps and heaters of the apparatus are initially inoperative, and the patient output heat exchanger 314 is initially drained of water.

Disinfection of the apparatus

The first stage of operation is the disinfection of the entire fluid circuit, starting with the water preparation module 200. For disinfection, the inlet valve 202 is opened so that water can flow into the isolator 208. The isolator air vent valve 209 is open to allow air from the isolator 208 to exit to atmosphere through the isolator air vent 17. The disinfectant selection valve 256 is positioned to direct the waste flow from the second RO membrane unit 252 through the disinfectant cartridge 210 and through the disinfection valve 212, which is open. The degassing pump 222 is operative and

draws fluid through the disinfection cartridge 210, or from the isolator 208 if insufficient fluid is available from the fluid path through the disinfection cartridge 210. The fluid from the disinfection cartridge 210 (or the isolator 208) passes to the thermal control and sterilisation module 300 via the cooling water output 2a and is preheated by the water heater 322 before being returned to the water preparation module 200 via the cooling water return connection 2b. The fluid then passes through the degassing components 214-224, which degas the fluid.

The RO pump 236 is operative to draw fluid from the degassing chamber 224 and pass the fluid through the first RO membrane unit 238. The first RO membrane bypass valve 250 is open so that waste fluid from the first RO membrane unit 238 is redirected to the output side of the RO membrane to continue the fluid path. No fluid from the first RO membrane unit 238 passes through the purification waste connection 2d, because the flow path through this connection is stopped by the thermal drain connection valve 520 in the drainage module 500. Disinfection fluid from the output side of the first RO membrane unit 238 passes through the RO pressure relief valve 260 and also past the second RO membrane unit 252 and is recirculated back to the disinfectant selection valve 256. Thus, it will be seen that a first disinfection loop is provided according to which water is circulated through the disinfection cartridge 210 to dilute the disinfectant and the diluted disinfectant is circulated through the majority of the water preparation module 200. None of the pumps in the thermal control and sterilisation module 300, the concentrate mixing module 400 or the drainage module 500 are operative during the initial disinfection of the water preparation module 200. There are therefore no components that pump fluid from the purified water connection 2c, such that a negligible amount of fluid crosses the second RO membrane unit 252 because there is no pressure differential across the membrane unit 252. Any fluid which does cross the second RO membrane unit 252 is routed to the external drain connection via the purified water connection 2c, the mixing water feed connection 4a, the mixing system

bypass valve 440, the mixing module output connection 4b, the OLA input valve 356, the sterile fluid connection 8a, the patient bypass valve 616, the sterilisation heat recovery bypass valve 618, the ambient pressure drain connection 14b, the heat recovery drain connection 13b, the heat recovery drain return connection 13c and the open heat recovery return valve 532. This water is replaced by water from the tap water inlet 1 via particle filter 204 and water softener 206.

During the first phase of disinfection of the water preparation module 200, the air bleed valve 320 in the thermal control and sterilisation module 300 is opened and the patient output heat exchanger pump 316 is operated to fill the patient output heat exchanger with disinfectant and to recirculate this disinfectant through the recirculation restrictor 310.

By closing the proportioning valve 214 completely with the degassing bypass valve 226 also closed, the flow through the cooling water return connection 2b is stopped. The patient output heat exchanger pump 316 is then used to pump disinfectant from the cooling water output 2a through the open air bleed valve 320, through the patient output heat exchanger vent connection 2e and into the isolator 208 to disinfect the patient output heat exchanger vent connection 2e. The isolator air vent valve 209 is closed during this process. The disinfectant from the isolator 208 continues to the cooling water output 2a of the water preparation module 200 to close this disinfectant circulation loop.

The patient output heat exchanger 314 can be drained of disinfectant by subsequently opening the isolator air vent valve 209 and the air bleed valve 320 while the patient output heat exchanger drain valve 318 is open and fluid is circulating between the cooling water output 2a and the cooling water return connection 2b when the patient output heat exchanger pump 316 is inoperative.

The air passage between the degassing chamber 224 and the isolator 208 is disinfected by closing the isolator air vent valve 209 and opening the degassing bypass valve 226. The degassing pump 222 is then operated with the RO pump 236 off such that the only flow from the degassing chamber 224 is

directly to the isolator 208 through the air passage.

At the end of the disinfection process, the disinfectant selector valve 256 is returned to its default position with the first RO membrane bypass valve 250 still open. Disinfectant is circulated by the RO pump 236 past the first RO membrane unit 238, the second RO membrane unit 252 and back round to the RO pump 236 via the second RO output restrictor 254 and the disinfectant selection valve 256. After this circulation, the first RO membrane bypass valve 250 is closed and the thermal drain connection valve 520 in the drainage module 500 is opened so that disinfectant can flow through the purification waste connection 2d to the thermal drain connection 13a and out of the external drain connection 16.

Finally, the water preparation module 200 is flushed with water to remove any remaining disinfectant along the disinfectant routes described above.

It will be seen from the above that the entire water preparation module 200 from the water softener 206 up to and including the second RO membrane unit 252 is chemically disinfected by the above process.

Downstream of the second RO membrane unit 252, water at disinfection temperature supplied from the RO membrane disinfection connection 3 is used to disinfect the fluid path between the second RO membrane unit 252 and the purified water connection 2c. In this case, water from the tap water connection 1 passes along the normal purification fluid path through the water preparation module 200 so that RO water is produced at the output side of the second RO membrane unit 252. The mixing water stop valve 442 of the concentrate mixing module 400 is opened and the salt input displacement pump 452 is energised to draw water from the mixing water feed connection 4a. The water supply to the mixing water feed connection 4a of the mixing module 400 is drawn from the purified water connection 2c of the water preparation module 200 and heated to disinfection temperature by the disinfection heater 330. The salt input displacement pump 452 pumps the water at disinfection temperature through the open RO membrane disinfection valve 499 to the output side of the second RO

membrane unit 252 via the RO membrane disinfection connection 3. Thus, a closed recirculation loop of water at disinfection temperature is provided, the temperature of which is monitored by the second RO temperature sensor 264.

The disinfection heat exchanger bypass valve 328 is disinfected as part of the above heat disinfection loop, by opening the valve to allow the hot disinfection water to pass there through.

The hot water is flushed to the drainage module 500 by deactivating the salt input displacement pump 452 and activating the flow control pump 446 to pump the hot water to the drainage module 500 via the mixing module drain connection 15.

Before the disposable concentrate container 402 is connected to the manifold 404, the manifold 404 and cap 406 are heat disinfected. To achieve this, the cap 406 is located on the manifold 404 to form a sealed cavity. The flow control pump 446 is activated to pump water heated to disinfection temperature by the disinfection heater 330 through the mixing water feed connection 4a. The flow control pump 446 pumps the disinfection water through the reservoir filling valve 466 and into the concentrate reservoir 468. The hot disinfecting fluid is pumped into the cavity formed by the manifold 404 and cap 406 sequentially in time through each of the reservoir vent disinfection valve 498, the reservoir output valve 470 and each of the salt input valves 478-488, so that all of these valves are disinfected. The cap air vent valve 474 vents air from the cavity formed by the manifold 404 and the cap 406 to the drainage module 500 via the mixing module drain connection 15. Once the manifold 404 and cap 406 are full of hot disinfection fluid, the fluid is forced through the mixing module drain connection 15 via the cap air vent valve 474 to the drainage module 500.

In the drainage module 500, the hot fluid passes out of the heat recovery drain connection 13b and through the disinfection heat exchanger 326. However, the disinfection heat exchanger bypass valve 328 is open so that no heat is lost from the disinfection fluid passing through the disinfection heat

exchanger 326 and returning to the drainage module 500 via the heat recovery drain return connection 13c. In this way, the heat recovery drain connection 13b and the heat recovery return valve 532 are also heat disinfected.

In order to disinfect the sodium bicarbonate air vent valve 492, water at disinfection temperature from the thermal control and sterilisation module 300 is drawn via the mixing water feed connection 4a by the salt input displacement pump 452. At this time, the only open fluid passages into the filled cavity formed by the manifold 404 and the cap 406 are via the sodium bicarbonate air vent valve 492 and the sodium bicarbonate input valve 482. Thus, as the salt input displacement pump 452 pumps hot water out of the cavity formed by the manifold 404 and the cap 406 via the sodium bicarbonate input valve 482 the hot water is replaced from the mixing water feed connection 4a via the sodium bicarbonate air vent valve 492. The sodium bicarbonate air vent valve 492 is toggled to disinfect the air vent and the fluid channel 428. The hot water is recirculated through this loop by closing the heat recovery return valve 532 in the drainage module 500 and opening the mixing water stop valve 442. The same method can be used to disinfect the sodium chloride air vent valve 494 and the sodium chloride input valve 484.

The fluid path to the glucose compartment 420 of the disposable concentrate container 402 is disinfected by using the flow control pump 446 to pump hot water from the thermal control and sterilisation module 300 via the mixing water feed connection 4a through the mixing system bypass valve 440, the glucose selector valve 444 and the glucose input valve 490 into the cavity formed by the manifold 404 and the cap 406. Subsequently, with the flow control pump 446 switched off, the glucose recirculation pump 448 is used to recirculate the hot water through the glucose output channel 436 and the fluid input channel 434. The glucose input valve 490 is closed at this stage. Finally, the hot disinfection fluid can exit the cavity formed by the manifold 404 and cap 406 via the cap air vent valve 474 and the mixing module drain connection 15.

After disinfection, the manifold 404 and cap 406 are

drained by connecting the cavity formed thereby to atmosphere at the air vent 6 by means of the cap air vent valve 474, and pumping the water out of the manifold and cap 406 using the salt input displacement pump 452 via the reservoir vent disinfection valve 498, the concentrate reservoir 468 and the reservoir output valve 470. The salt input displacement pump 452 pumps the water to the drainage module via the flow control pump bypass valve 458, the drain disinfection valve 464 and the mixing module drain connection 15.

In order to disinfect the thermal control and sterilisation module 300 and the cycler and sterilisable connector module 600, hot water is pumped by the volumetric pump 352 from the disinfection heater 330 via the mixing water feed connection 4a, the mixing system bypass valve 440 and the mixing module output connection 4b through the OLA input valve 356. In a further route, the disinfection fluid is pumped through the OLA sterilisation valve 376. The disinfection fluid passes through the thermal control and sterilisation module 300 to the sterile fluid connection 8a and then through the patient fill valve 602, through the chamber 632 and fluid passage 640 of the sterilisable connector 604, the patient drain cut-off valve 606, the sterilisation bypass valve 614 the sterilisation heat recovery bypass valve 618 and into the drainage module 500 via the ambient pressure drain connection 14b.

In a further disinfection route, the disinfection fluid entering the cycler and sterilisable connector module 600 through the sterile fluid connection 8a, passes through the patient bypass valve 616, and through the sterilisation heat exchanger 378 via the sterilisation output connection 8b. At this time, there is no fluid flow through the other side of the sterilisation heat exchanger 378 and thus no heat is lost from the disinfection fluid during its passage through the sterilisation heat exchanger 378. The disinfection fluid entering the cycler and sterilisable connector module 600 via the sterilisation fluid return connection 8c passes to the drainage module 500 via the ambient pressure drain connection 14b.

In the final disinfection route through the cycler and

sterilisable connector module 600, hot disinfection fluid from the sterile fluid connection 8a passes through the patient fill valve 602, the sterilisable connector 604, the patient drain cut-off valve 606, the first patient drain valve 608 and onward to the negative pressure drain connection 14a. At this time, the drainage pump 508 is operative.

It will be seen from the above that the whole fluid system from the water softener 206 to the patient pinch valves 624, including the drainage module 500 can be disinfected either chemically or by heat disinfection.

Cleaning and Flushing

After disinfection, the disposable concentrate container 402 is connected to the manifold 404, and a downstream cleaning operation is then carried out.

For the cleaning operation, RO water preheated by the disinfection heater 330 to mixing temperature is drawn into the concentrate mixing module 400 by the salt input displacement pump 452 via the mixing water stop valve 442 and directed through the cleaning agent input valve 480 into the cleaning agent compartment 410 of the concentrate disposable container 402. Sufficient water is pumped into the cleaning agent compartment 410 to dissolve all of the powdered cleaning agent stored therein. Once the cleaning agent is dissolved, the salt input displacement pump 452 is reversed to draw the cleaning agent solution out of the cleaning agent compartment 410 through the cleaning agent input valve 480. The cleaning agent is pumped into the concentrate reservoir 468 via the reservoir filling valve 466 by the salt input displacement pump 452. From the concentrate reservoir 468, the cleaning agent is passed to the drainage module 500 via the reservoir air vent valve 496 and the mixing module drain connection 15.

For cleaning of the downstream components in the thermal control and sterilisation module 300 and the cycler and sterilisable connector module 600, the cleaning agent is pumped by the salt input displacement pump 452 through the flow control pump bypass valve 458 and the reservoir filling valve 466 to the mixing module output connection 4b. The flow of

cleaning agent is directed through the thermal control and sterilisation module 300 and the cycler and sterilisable connector module 600 according to any of the disinfection routes described above.

After cleaning, the thermal control and sterilisation module 300 and the cycler and sterilisable connector module 600 are flushed with purified water from the water preparation module 200 to remove any remaining cleaning agent.

The cleaning agent may be sodium carbonate, but other cleaning agents may be used, such as citric acid, or precursors for a cleaning agent.

Treatment

Once the fluid system has been disinfected, cleaned and flushed, the first stage of the treatment process is the dissolution of the salts and glucose in the concentrate disposable container 402. Thus, RO water at mixing temperature is pumped by the salt input displacement pump 452 through the mixing water stop valve 442 sequentially into each of the salt compartments 412-418 through the respective input valves 482-488. Sufficient water is pumped by the salt input displacement pump 452 to fill the respective compartment 412-418 of the concentrate disposable container 402, but the volume of fluid pumped by the salt input displacement pump 452 is carefully monitored to ensure that too much water is not input into the compartment 412-418 which would overflow through the air vent channel 424,428. Once each compartment 412-418 is full, the respective input valve 482-488 is closed while the salt dissolves. The volumes of water input into the compartments 408,412-418 are carefully selected. Thus, the control system knows how much water is in each compartment. If too much water is introduced into the sodium bicarbonate 412 or the sodium chloride compartment 414 no harm is done because the resultant solution will still be substantially saturated.

For filling of the glucose compartment 420, RO water at mixing temperature, for example 37°C, is pumped by the flow control pump 446 from the mixing water feed connection 4a via the mixing system bypass valve 440, the reservoir filling valve

466 and the glucose selector valve 444 through the open glucose input valve 490 into the glucose compartment 420 via the fluid input channel 434. The glucose recirculation pump 448 is deactivated at this stage. Once sufficient fluid has been pumped into the glucose compartment 420 to fill that compartment to a level not exceeding the top of the glucose air vent channel 432, the glucose input valve 490 is closed and the glucose recirculation pump 448 recirculates the glucose solution to aid dissolution. The volume of water pumped into the glucose compartment 420 determines the concentration of the glucose solution.

While the glucose and salts are dissolving, the patient fluid circuit is sterilised. Thus, RO water is drawn by the volumetric pump 352 from the mixing water feed connection 4a through the mixing system bypass valve 440 and the mixing module output connection 4b and is pumped through the OLA sterilisation valve 376. The water passes through the sterilisation heat exchanger 378, where it is preheated, and then through the second OLA heat exchanger 362 for further preheating. The volumetric pump 352 pressurises the water to a sufficiently high pressure that the OLA heating bath 364 can raise the temperature of the water to a suitable sterilisation temperature, i.e. above 100°C, preferably above 121°C, without boiling. The heated pressurised water passes through the hot side of the second OLA heat exchanger 362 and of the first OLA heat exchanger 360. However, because there is no flow through the cold side of the first OLA heat exchanger 360, no heat is transferred from the heated pressurised water. Similarly, as the heated pressurised water passes through the patient output heat exchanger 314, no heat is transferred because the water bath in the patient output heat exchanger 314 has been drained. The heated pressurised water passes through the patient output pressure relief valve 374, which is deactivated so that there is no drop in pressure, and enters the cycler and sterilisable connector module 600 via the sterile fluid connection 8a.

In the cycler and sterilisable connector module 600 the heated pressurised water firstly passes through the patient fill valve 602, the sterilisable connector 604, the patient

drain cut-off valve 606 and the sterilisation bypass valve 614 to the sterilisation output connection 8b. The first patient drain valve 608 is closed during this operation to protect the patient drain pressure sensors 610 from the elevated pressure and the output volumetric flow meter 650 from the elevated temperature. Thus, the fluid path between the first patient drain valve 608 and the drainage module 500 is not sterilised. However, this line has been disinfected and does not handle fluid which is subsequently passed to the patient, so that there is no risk to the patient. From the sterilisation output connection 8b the heated pressurised water passes through the sterilisation heat exchanger 378 where its temperature is reduced by heat transfer to the relatively cool water passing through the OLA sterilisation valve 376. The cooled pressurised water then passes via the sterilisation fluid return connection 8c through the sterilisation pressure relief valve 620 which reduces the pressure to atmospheric. The cooled ambient pressure water passes through the sterilisation return shut-off valve 622, through the ambient pressure drain connection 14b and the heat recovery drain connection 13b to the disinfection heat exchanger 326 where the temperature of the water is further reduced before the water is passed to the external waste connection 16 via the heat recovery drain return connection 13c and the heat recovery return valve 532.

During a further stage of the sterilisation of the cycler and sterilisable connector module 600 the patient fill valve 602 and the sterilisation bypass valve 614 are closed so that the high temperature pressurised water can pass through the patient bypass valve 616 (which is now open) to the sterilisation output connection 8b to sterilise the patient bypass valve 616.

In the above manner, it is ensured that the fluid circuit from the OLA heating bath 364 to the sterilisation heat exchanger 378 is sterile. The sterility is maintained throughout the treatment session.

Once the fluid path from the OLA 375 to the sterilisable connector 604 has been sterilised, sterile fluid is passed along this path continuously until the end of the treatment

session to maintain sterility. The fluid may be water from the water preparation module 200 which passes from the mixing water feed connection 4a through the mixing system bypass valve 440 to the mixing module output connection 4b, through the OLA 375, where it is sterilised and then through the patient bypass valve 616 and the sterilisation heat recovery bypass valve 618 to the drainage module 500. Alternatively, the fluid may be PD fluid from the concentrate mixing module 400 which is sterilised in the OLA 375 and passed to the drainage module 500 along the same fluid path as described above. In this way, the OLA 375 can operate continuously without overheating to ensure sterility at all times. When the PD fluid is to be delivered to the patient, the patient bypass valve 616 is shut and the patient fill valve 602 is opened to allow the PD fluid to pass to the sterilisable connector 604.

Once the sterilisation operation has been completed, the concentrated PD fluid is mixed in the concentrate reservoir 468 in the manner described in detail above in relation to the concentrate mixing module 400.

While the concentrated PD fluid is being mixed, the water bath of the patient output heat exchanger 314 is filled by opening the air bleed valve 320 and activating the patient output heat exchanger pump 316, in preparation for delivery of PD fluid to the patient.

The apparatus is now ready for the arrival of the patient. When the patient arrives, the membranes 634 on the disposable fluid line 10 are pierced by the sterilisable connector 604. The disposable fluid line 10 is primed by pumping PD fluid (or sterile water) from the mixing module output connection 4b through the OLA input valve 356 using the volumetric pump 352. The PD fluid is produced in the mixing module 400 by diluting the concentrated PD fluid pumped by the salt input displacement pump 452 from the concentrate reservoir 468 to the mixing chamber 450 with a flow of purified water from the water preparation module 200. The flow control pump 446 is bypassed during delivery of the PD fluid by opening the flow control pump bypass valve 458. The PD fluid passes through the first OLA heat exchanger 360, the second OLA heat exchanger

362 and the OLA heating bath 364 and is thereby sterilised. The sterilised PD fluid is brought down to the required patient temperature by the patient output heat exchanger 314 and is depressurised by the patient output pressure relief valve 374. The sterile PD fluid is then passed through the patient fill valve 602 and the patient pinch valve 624 into the disposable dialysate line 10. The PD fluid passes through the disposable fluid line 10 and returns to the sterile connector 604 via the second patient pinch valve 624. The returned fluid passes through the patient drain cut-off valve 606 and the first patient drain valve 608. The output volumetric flow meter 650 registers the fluid flow and confirms that the disposable fluid line 10 has been successfully primed with PD fluid. The PD fluid then passes to the drainage module 500 via the negative pressure drain connection 14a. In this way, it is ensured that there is only a minimal amount of air in the disposable dialysate line which connects to the patient's peritoneal cavity.

Once the disposable fluid line 10 has been primed, the patient is invited to connect to the disposable fluid line 10 so that any fluid in the patient's peritoneal cavity can be drained. During draining of the patient the drainage pump 508 is activated to draw dialysate from the sterilisable connector 604 through the patient drain cut-off valve 606 and past the output volumetric flow meter 650 to the negative pressure drain connection 14a. The output volumetric flow meter 650 records the volume of dialysate withdrawn from the patient's cavity. During drainage, a sample of the patient's dialysate may be taken by the sampling module 700.

In the case of subsequent filling and draining of the patient's cavity, additional concentrated PD fluid is mixed by the mixing module 400 in the concentrate reservoir 468 while the patient is being drained by the cycler and sterilisable connector module 600 and the drainage module 500.

When the patient's peritoneal cavity is empty, which is registered by a drop in pressure or flow rate detected by the patient drain pressure sensor 610 or the output volumetric flow meter 650, or when a predetermined drain time has elapsed, the

drainage pump 508 is deactivated. The patient's peritoneal cavity can then be filled with sterile PD fluid from the sterile fluid connection 8a of the thermal control and sterilisation module 300 via the patient fill valve 602, the sterilisable connector 604 and the patient pinch valve 624. During filling of the patient, the pressure of the PD fluid entering the patient is monitored using the pressure tap described in detail above in relation to the cycler and sterilisable connector module 600. The volume of PD fluid entering the patient's peritoneal cavity is recorded by the input volumetric flow meter 350.

Once sufficient fluid has been passed to the patient, the fluid system downstream of the mixing module output connection 4b is flushed through to the drainage module 500 firstly with the remaining PD fluid (which is sterilised) and then with sterilised water to remove any glucose deposits that remain in the OLA 375 and would caramelise. The system then awaits drainage of the patient. Thus, a cycle of drains and fills can be repeated over an extended period to complete a treatment session.

At the end of a treatment session, once the patient has disconnected from the apparatus 100, any remaining salt or glucose solutions in the concentrate disposable container 402 are pumped to the drainage module via the mixing module drain connection 15. The fluid system is then flushed with clean water utilising the disinfection routes described above. The concentrate disposable container 402 and the disposable fluid line 10 are replaced. Finally, the system is cleaned as described above and then flushed with clean water, before the system is shut by closing the inlet valve 202, the thermal drain connection valve 520 and the heat recovery return valve 532. The apparatus is then ready for the next treatment session.

During extended periods of non-use, the entire fluid system may be filled by an engineer with a suitable preservative and closed to atmosphere to prevent bacteriological build-up.

It is mentioned that the apparatus has a memory device

capable of storing information for later retrival. Such a memory device may be a hard disk or a solid state memory device. Parameters to be stored in a technical log may be selected from the following non-exhaustive list: time and result of processes, like cleaning, sterlilisation, verification of sterility; flow rates; conditions of valves, pumps; pump speeds; sensor values such as conductivities, temperatures, pressures, temperatures.

It will be apparent to those skilled in the art that various modifications and variations can be made to the structure and methodology of the present invention without departing from the scope or spirit of the invention. For example, certain aspects of the structure and methodology of the invention which have been particularly described in relation to peritoneal dialysis could be used for acute dialysis, home dialysis, chronic dialysis in general including hemodialysis or hemofiltration or hemodiafiltration or any other medical fluid production or treatment procedure (including producing nutritional solutions) especially those involving infusion and/or removal of fluids to and/or from a patient. Thus, it should be understood that the invention is not limited to the examples discussed in this specification and shown in the drawings. Rather, the invention is intended to cover modifications and variations provided they come within the scope of the following claims and their equivalents.

Claims

1. Apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:

a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;

a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;

a steriliser arranged to sterilise at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a patient,

characterised in that

at least one of the concentrates is in substantially dry form and, in use of the apparatus, is at least partially dissolved to form part of the peritoneal dialysis fluid.

2. Apparatus as claimed in claim 1, **characterised** in that in one of the chambers the concentrate is an osmotic agent in substantially dry form.

3. Apparatus as claimed in claim 2, **characterised** in that the osmotic agent is glucose.

4. Apparatus as claimed in claim 1, 2 or 3, **characterised** in that each concentrate comprises a single concentrate substance.

5. Apparatus as claimed in any preceding claim, **characterised** in that each of said chambers contains a separate constituent substance of the peritoneal dialysis fluid, selected from a group comprising: sodium chloride, sodium bicarbonate, magnesium chloride, calcium chloride, sodium lactate, lactic acid and glucose.

6. Apparatus as claimed in claim 5, **characterised** in that

the concentrates comprise: sodium chloride in substantially dry form; sodium bicarbonate in substantially dry form; magnesium chloride in substantially dry form; calcium chloride in substantially dry form; lactic acid solution; and glucose in substantially dry form.

7. Apparatus as claimed in any preceding claim, **characterised** by a chamber containing a cleaning agent.

8. Apparatus as claimed in any preceding claim, **characterised** by a controller for controlling the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other.

9. Apparatus as claimed in claim 8, **characterised** in that the concentrates comprise a plurality of electrolytes, and wherein the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative electrolyte concentrations from each other.

10. Apparatus as claimed in claim 8 or 9, **characterised** in that the controller has data input means for receiving prescription information for a patient.

11. Apparatus as claimed in any preceding claim, arranged to prime said at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is only partially dissolved when the chamber is filled with liquid, **characterised** in that the apparatus further comprising a flow line for removing liquid comprising dissolved concentrate from the chamber, and a flow line for substantially simultaneously adding the same amount of liquid as removed to said chamber.

12. Apparatus as claimed in claim 11, **characterised** in that the concentrate removal flow line is used during priming to introduce the liquid comprising water to the chamber, and the

liquid adding flow line is used during priming to vent air from the chamber.

13. Apparatus as claimed in claim 11 or 12, **characterised** in that the at least one concentrate in the partial dissolution chamber is selected from a group comprising sodium chloride and sodium bicarbonate.

14. Apparatus as claimed in any of claims 1 to 10, arranged to prime said at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, **characterised** in that the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is fully dissolved when the chamber is filled with liquid.

15. Apparatus as claimed in claim 14, **characterised** in that the at least one concentrate in the full dissolution chamber is selected from a group comprising magnesium chloride and calcium chloride.

16. Apparatus as claimed in any of claims 1 to 10, **characterised** in that said at least one concentrate in substantially dry form comprises at least a first and a second concentrate in substantially dry form and wherein:

said first concentrate is in a first chamber and said apparatus is arranged to prime said first concentrate in substantially dry form with liquid comprising water, the amount of first concentrate in the first chamber and the size of the chamber being such that the first concentrate is only partially dissolved when the first chamber is filled with liquid, the apparatus further comprising a flow line for removing liquid comprising dissolved concentrate from the first chamber, and a flow line for substantially simultaneously adding the same amount of liquid as removed to said first chamber, and

said second concentrate is in a second chamber and said apparatus is arranged to prime said second concentrate in substantially dry form with liquid comprising water, the amount of second concentrate in the second chamber and the size of the

second chamber being such that the second concentrate is fully dissolved when the second chamber is filled with liquid.

17. Apparatus as claimed in any preceding claim, **characterised** in that a respective chamber contains an osmotic agent and wherein the apparatus comprises a flow circuit for introducing liquid comprising water into the osmotic agent chamber, for removing liquid comprising dissolved osmotic agent from the osmotic agent chamber and for re-introducing the liquid comprising dissolved glucose into the osmotic agent chamber.

18. Apparatus as claimed in claim 17, **characterised** in that a heater for heating the liquid comprising dissolved osmotic agent as it circulates round the flow circuit.

19. Apparatus as claimed in claim 18 or 19, **characterised** by a vent to allow escape of gas as the liquid comprising dissolved osmotic agent circulates round the flow circuit.

20. Apparatus as claimed in any of claims 17 to 19 **characterised** in that the osmotic agent comprises glucose.

21. Apparatus as claimed in any preceding claim, **characterised** in that the steriliser is a heat steriliser for sterilising the peritoneal dialysis fluid at elevated pressure.

22. Apparatus as claimed in claim 21, **characterised** in that the heat steriliser is provided downstream of the fluid mixer.

23. Apparatus as claimed in any preceding claim, **characterised** in that the liquid is chosen from the group of water and purified water.

24. Apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:

a plurality of chambers each containing a respective

concentrate of a constituent of the peritoneal dialysis fluid;

a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;

a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;

a steriliser arranged to sterilise at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a patient,

characterised in that

the controller has data input means for receiving predetermined prescription information for a patient and in that the controller is operable to control the fluid mixer to produce a peritoneal dialysis fluid formulation based on the received predetermined prescription information.

25. Apparatus as claimed in claim 24, **characterised** in that the concentrates comprise a plurality of electrolytes and wherein the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative electrolyte concentrations from each other.

26. Apparatus as claimed in claim 24 or 25, **characterised** in that the chambers are in the form of compartments of a container, and wherein all the concentrates required to make a said peritoneal dialysis formulation are provided in said compartments.

27. Apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:

a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;

a fluid mixer arranged to mix the concentrates with liquid to produce the peritoneal dialysis fluid;

a controller arranged to control the fluid mixer

selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;

a steriliser arranged to sterilise at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal dialysis of a patient;

characterised in that

the concentrates comprise a plurality of electrolytes, and in that the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes.

28. Apparatus as claimed in any of claims 24 to 27, **characterised** in that the liquid is chosen from the group of water and purified water.

29. Apparatus as claimed in any preceding claim, **characterised** in that the plurality of chambers are defined by a single container.

30. Apparatus as claimed in claim 29, **characterised** by a container engaging portion for engaging the container and urging it to a position in which the chambers are opened for communication with respective portions of the apparatus.

31. Apparatus as claimed in claim 30, **characterised** in that each chamber has means defining an opening thereof and a flange provided adjacent said opening, and wherein the container engaging portion is arranged to engage the flanges adjacent the openings.

32. Apparatus as claimed in claim 31, **characterised** in that the openings are linearly aligned with each other, and wherein the container engaging portion comprises a pair of laterally spaced members arranged to engage said flanges defined on opposite sides of the openings.

33. Apparatus as claimed in any of claims 29 to 32, **characterised** in that said chamber has a seal penetrable to open said chamber, the apparatus further comprising a plurality of spikes for penetrating the respective seals of the chambers to open said chambers.

34. Apparatus as claimed in claim 33, **characterised** in that a said spike comprises two fluid flow channels.

35. Apparatus as claimed in claims 33 or 34, **characterised** by a pair of spikes for penetrating an osmotic agent containing chamber, thereby providing at least three fluid flow channels.

36. Apparatus as claimed in claims 33, 34 or 35, **characterised** by a cover for covering a said spike when the container is removed to enable the spike to be disinfected.

37. Apparatus as claimed in claim 36 when dependent on claim 30, **characterised** in that the container engaging portion is arranged to engage the cover to urge it to its covering position.

38. Apparatus as claimed in any preceding claim, **characterised** in that it comprising a water purifier, wherein the water purifier comprises a first reverse osmosis membrane unit, and a second reverse osmosis membrane unit, each membrane unit having an inlet, a purified water outlet and a waste water outlet, wherein the purified water outlet of the first membrane unit is in fluid communication with the inlet of the second membrane unit and the waste water outlet of the second membrane unit is in fluid communication with the inlet of the first membrane unit.

39. Apparatus as claimed in claim 38, **characterised** in that the water purifier further comprises at least one of a coarse filter, a water softener and a fine filter upstream of the inlet of the first reverse osmosis membrane unit.

40. Apparatus as claimed in claim 38 or 39, **characterised** in that the water purifier further comprises a degassing arrangement upstream of the inlet of the first reverse osmosis membrane unit.

41. Apparatus for the production of peritoneal dialysis fluid at a treatment location comprising:

a water inlet arranged to receive water from a water supply;

a water purifier arranged to purify the water from the water inlet;

a fluid mixer arranged to mix dialysis fluid concentrate with the purified water to produce peritoneal dialysis fluid;

a steriliser arranged to sterilise the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the sterilised supply of peritoneal dialysis fluid to the peritoneal cavity of a patient,

characterised in that

the steriliser is a heat steriliser arranged for heat sterilisation of the peritoneal dialysis fluid at a sterilising temperature and at an elevated pressure.

42. Apparatus as claimed in claim 41, **characterised** in that the heat steriliser is provided downstream of the fluid mixer.

43. Apparatus as claimed in any preceding claim, **characterised** in that the steriliser comprises a sterilisation flow passage and is arranged to heat sterilise the peritoneal dialysis fluid as it flows along the sterilisation flow passage.

44. Apparatus as claimed in claim 43, **characterised** by a flow path downstream of the heat steriliser for the flow of sterilised peritoneal dialysis fluid to the patient fill connection, and a dialysis fluid cooler arranged to cool the sterilised peritoneal dialysis fluid as it flows along the flow path.

45. Apparatus as claimed in claim 44, being arranged to heat sterilise the flow path prior to its use for the flow of sterilised peritoneal dialysis fluid to the patient fill connection.

46. Apparatus as claimed in any preceding claim, characterised in that the steriliser is arranged to heat the peritoneal dialysis fluid to a temperature of at least about 140°C.

47. Apparatus as claimed in any preceding claim, characterised in that the steriliser is arranged to heat the peritoneal dialysis fluid to obtain an F_0 value of at least about 20 minutes where F_0 is given by:

$$F_0 = \int_0^L \frac{S}{Q} \times 10^{\left(\frac{T(y)-121}{10}\right)} dy$$

where:

L represents the length of a sterilisation fluid path for the peritoncal dialysis fluid;

S represents the internal cross-sectional area of the sterilisation fluid path;

Q represents the volume flow rate of the peritoneal dialysis fluid along the sterilisation fluid path; and

T(y) represents the temperature distribution of the peritoneal dialysis fluid as a function of the distance from the start of the sterilisation fluid path.

48. Apparatus for the production of an aqueous solution for medical use from a plurality of concentrates, the apparatus being arranged to communicate with a plurality of chambers each containing a respective concentrate, at least one of the concentrates being in substantially dry form, the apparatus comprising:

at least one flow line arranged to prime said at least one concentrate in substantially dry form with liquid

comprising water to form at least one dissolved concentrate;

a mixing vessel arranged to receive the at least one dissolved concentrate;

a flow regulator associated with the at least one dissolved concentrate arranged to pass the concentrate to the mixing vessel;

characterised by

measuring means arranged to measure a concentration of the at least one dissolved concentrate; and

a pump arranged to pump a metered volume of the at least one dissolved concentrate via the associated flow regulator to said mixing vessel, whilst measuring by said measuring means the concentration of the dissolved concentrate, so as to deliver a predetermined amount of said dissolved concentrate to said mixing vessel.

49. Apparatus as claimed in claim 48, **characterised** by a flow regulator associated with each concentrate wherein in use of the apparatus a metered volume of each concentrate is pumped via its associated flow regulator to the mixing vessel, whilst measuring the concentration of the concentrate, so as to deliver a predetermined amount of the concentrate to the mixing vessel.

50. Apparatus as claimed in claim 48 or 49, **characterised** in that the pump is arranged to pump, in turn, each concentrate in liquid form to the mixing vessel.

51. Apparatus as claimed in claim 48, 49 or 50, **characterised** in that the measuring means is arranged to measure, in turn, the concentration of each concentrate.

52. Apparatus as claimed in any of claims 48 to 51, **characterised** in that it is arranged to dilute a concentrate after it leaves its respective chamber and before it is passed to the mixing vessel.

53. Apparatus as claimed in claim 52, **characterised** by a

concentrate flow line along which concentrate is pumped by the pump at a metered rate, a water flow line along which water is pumped by a second pump at a metered rate, the concentrate flow line joining the water flow line so that in use the concentrate and water are mixed to dilute the concentrate before it is passed to the mixing vessel.

54. Apparatus as claimed in claim 53, **characterised** in that the measuring means is arranged to measure the concentration of the concentrate or diluted concentrate, and wherein in use the pumps are controlled to provide a dilution ratio required in order to obtain a desired concentration of the diluted concentrate.

55. Apparatus as claimed in claim 52, 53 or 54, **characterised** in that it is arranged to pass the diluted concentrate to the mixing vessel at a flow rate by means of said pump, whilst measuring by said measuring means the concentration of the diluted concentrate, and wherein the apparatus comprises a processor for multiplying the measured concentration with said flow rate, for integrating the product of said multiplication over time to obtain a total amount of concentrate material delivered to said mixing vessel, and for terminating said passing of diluted concentrate to said mixing vessel when a predetermined amount of concentrate material has been delivered to the mixing vessel.

56. Apparatus as claimed in any of claims 48 to 55, **characterised** in that in use the apparatus is arranged to measure a property of a said concentrate or a property of the concentrate after dilution thereof downstream of its respective chamber, and wherein the apparatus comprises a checking device for determining from that measurement if the concentrate is the concentrate expected from that chamber.

57. Apparatus as claimed in any of claims 48 to 56, **characterised** in that in use the liquid in the mixing vessel is passed towards a point of use and is diluted downstream of the

mixing vessel.

58. Apparatus as claimed in claim 57, **characterised** in that said measuring means which is used to measure the concentration of the concentrates delivered to the mixing vessel is also used to measure the concentration of the concentrates in the diluted liquid downstream of the mixing vessel.

59. Apparatus as claimed in any of claims 48 to 58, **characterised** in that the pump is reversible and connectible to a source of liquid, such that in use of the apparatus, after termination of delivery of a said concentrate, the pump is reversed to pump said liquid from the source thereof through the associated flow regulator so as to flush the path between the liquid source and the valve.

60. A method of providing an aqueous solution for medical use from a plurality of concentrates, comprising:

providing a plurality of concentrates in separate chambers, at least one of the concentrates being in substantially dry form;

priming said at least one concentrates in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

passing the at least one dissolved concentrate to a mixing vessel via a flow regulator associated with that concentrate;

characterised by

adjusting the flow regulator associated with the at least one dissolved concentrate for passing a metered volume of said concentrate through said flow regulator;

measuring a concentration of said concentrate to determine an amount of said concentrate delivered to said mixing vessel; and

terminating said delivering of concentrate when a predetermined amount has been delivered.

61. A method as claimed in claim 60, **characterised** by

adjusting a first flow regulator associated with a first concentrate for passing the first concentrate through the first flow regulator at a metered rate, measuring a concentration of the first concentrate to determine an amount of said concentrate delivered to said mixing vessel, terminating said delivering of said first concentrate when a predetermined amount has been delivered, adjusting a second flow regulator associated with a second concentrate for passing the second concentrate through the second flow regulator at a metered rate, measuring a concentration of the second concentrate to determine an amount of said concentrate delivered to said mixing vessel, terminating said delivering of said second concentrate when a predetermined amount has been delivered, and repeating said adjusting, passing, measuring and terminating for each further concentrate, thereby to provide an aqueous solution comprising a predetermined amount of each concentrate.

62. A method as claimed in claim 60 or 61, **characterised** in that the metered volume is passed using a pump, and the same pump is used to pump, in turn, each concentrate to the mixing vessel.

63. A method as claimed in claim 60, 61 or 62, **characterised** by using the same measuring means to measure, in turn, the concentration of each concentrate.

64. A method as claimed in any of claims 60 to 63, **characterised** by diluting a said concentrate after it leaves its respective chamber and before it is passed to the mixing vessel.

65. A method as claimed in claim 64, **characterised** by passing a said concentrate along a concentrate flow line by means of the pump at a metered rate, passing water along a water flow line by means of a second pump at a metered rate, and mixing said concentrate supplied along said concentrate line with said water supplied along said water line to provide

a diluted concentrate.

66. A method as claimed in claim 65, **characterised** by measuring the concentration of the concentrate or diluted concentrate, and controlling the pumps to provide a dilution ratio required in order to obtain a desired concentration of the diluted concentrate.

67. A method as claimed in claim 64, 65 or 66, **characterised** by passing said diluted concentrate to the mixing vessel at a flow rate, measuring the concentration of the diluted concentrate, multiplying said measured concentration with said flow rate, integrating the product of said multiplication over time to obtain a total amount of concentrate material delivered to said mixing vessel, and terminating said passing of diluted concentrate to said mixing vessel when a predetermined amount of concentrate material has been delivered to said mixing vessel.

68. A method as claimed in any of claims 60 to 67, **characterised** by measuring a property of a said concentrate or a property of the concentrate after dilution thereof downstream of its respective chamber, and determining from that measurement if the concentrate is the concentrate expected from that chamber.

69. A method as claimed in any of claims 60 to 68, **characterised** by passing the liquid in the mixing vessel towards a point of use and diluting said liquid downstream of the mixing vessel.

70. A method as claimed in claim 69, **characterised** by measuring the concentration of the concentrates in the diluted liquid using the same measuring means as is used to measure the concentration of the concentrates during delivery to the mixing vessel.

71. A method as claimed in any of claims 60 to 70,

characterised by, after terminating said delivery of a said concentrate, reversing the direction of the pump and pumping liquid from a source thereof through the associated valve so as to flush the path between the liquid source and the valve.

72. A container comprising a plurality of chambers each containing a respective concentrate of peritoneal dialysis fluid, for use in apparatus as claimed in any of claims 1 to 47.

73. A container comprising a plurality of chambers each containing a respective concentrate, for use with apparatus as claimed in any of claims 48 to 59.

74. A container containing in concentrated form all the concentrates, which when mixed with water, provide sufficient peritoneal dialysis fluid for a full peritoneal dialysis treatment session.

75. A container containing concentrated components of dialysis fluid, the container comprising a chamber containing powdered glucose and at least one other distinct chamber containing an inorganic salt in substantially dry form.

76. A container containing concentrated components of dialysis fluid, the container at least one chamber containing a cleaning agent and at least one other distinct chamber containing a powdered inorganic salt.

77. A container containing concentrated components of dialysis fluid, the container comprising defined therein at least two distinct chambers, each of said chambers containing a different inorganic salt, wherein the volume of each of said chambers and the amount of salt contained within each chamber is such that when a solution of each salt is prepared by filling each of said chambers with liquid, the conductivities of the solutions so prepared are characteristically different.

78. A container containing concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein each said connector comprises at least two separate fluid channels, permitting simultaneous inflow to and outflow from the respective chamber.

79. A container as claimed in claim 78, wherein said at least two fluid channels are arranged concentrically in each of said connectors.

80. A container as claimed in claim 78 or 79, wherein at least one of said chambers comprises two connectors, one such connector comprising said at least two separate flow channels, and the other connector comprising a further fluid channel.

81. A container as claimed in claim 78, 79 or 80, wherein the connectors are provided in a lower region of the chambers, and wherein one of the fluid channels of at least one connector has a portion extending to an upper region of the chamber.

82. A container as claimed in any of claims 78 to 81, wherein one of the fluid channels of a respective chamber is provided with a diffuser to diffuse an inflow of liquid into the chamber.

83. A container as claimed in any of claims 78 to 82, wherein the connectors are mutually aligned along a linear axis.

84. A container as claimed in claim 83, wherein the linear axis of the mutually aligned connectors is offset from a central axis of the container.

85. A container for use in priming powdered glucose at a patient treatment location, comprising an inlet port in a lower region of the container for receiving a supply of water to dissolve the powdered glucose in the container, wherein said

inlet port is provided with a diffuser which is arranged to diffuse the flow of water into the powdered glucose.

86. A container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein said connectors are mutually aligned along a linear axis.

87. A container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising a container body and at least one connector associated with each chamber, wherein there is at least one axis about which the container body is substantially rotationally symmetric, wherein the connectors are arranged relative to said container body such that the arrangement of connectors is rotationally asymmetric about said axis.

88. A method of manufacturing a container for concentrated components of dialysis fluid, the method comprising the steps of:

manufacturing a plurality of individual sub-containers; and

connecting said sub-containers to form said container.

89. A container for concentrated components of dialysis fluid manufactured according to the method of claim 88.

90. A universal container for patients having differing dialysis treatment requirements, the container comprising:

a plurality of compartments containing amounts of chemical components capable of being combined with liquid to form dialysis solution, wherein the amounts of the chemical components are sufficient to form a plurality of differing formulations of dialysis solution for a plurality of differing patient prescriptions; and

at least one port for placing the compartments in fluid

communication with a dialysis treatment system.

91. A universal container for use with a dialysis system and for patients having differing dialysis treatment requirements, the container comprising:

a first compartment;

a second compartment;

a third compartment;

a fourth compartment;

a fifth compartment;

a first port in flow communication with the first compartment;

a second port in flow communication with the second compartment;

a third port in flow communication with the third compartment;

a fourth port in flow communication with the fourth compartment;

a fifth port in flow communication with the fifth compartment;

a first chemical composition in the first compartment, capable of being combined with liquid to form a first constituent of dialysis solution;

a second chemical composition in the second compartment, capable of being combined with liquid to form a second constituent of dialysis solution;

a third chemical composition in the third compartment, capable of being combined with liquid to form a third constituent of dialysis solution;

a fourth chemical composition in the fourth compartment, capable of being combined with liquid to form a fourth constituent of dialysis solution; and

a fifth chemical composition in the fifth compartment, capable of being combined with liquid to form a fifth constituent of dialysis solution,

wherein the first, second, third, fourth, and fifth chemical compositions are provided in quantities sufficient to fill a plurality of differing patient prescriptions.

92. A container for use in a dialysis treatment session for a patient, comprising:

a plurality of compartments;

a plurality of quantities of differing chemical compositions contained in the compartments, the chemical compositions being capable of being combined with liquid to form constituents of dialysis solution, the quantities of the chemical compositions being sufficient to provide a plurality of patient prescriptions for dialysis solution, and the quantities being such that a substantial amount of at least one chemical composition does not become part of the dialysis solution and is not infused to a patient;

at least one port in flow communication with the compartments.

93. A container for use with a dialysis system, the container comprising:

a first compartment containing calcium chloride;

a second compartment containing magnesium chloride;

a third compartment containing sodium chloride;

a fourth compartment containing a cleaning agent;

a fifth compartment containing sodium bicarbonate;

a sixth compartment containing glucose, and

a plurality of ports associated with the compartments and connectable to a dialysis treatment unit at a patient treatment location, to thereby permit dialysis liquid to be constituted at the patient treatment location.

94. The container of claim 93, wherein the contents of at least some of the compartments are in substantially dry form, and wherein at least some of the plurality of ports are configured to receive liquid there through for mixing with the substantially dry contents to form solutions in the respective compartments.

95. The container of claim 93, further comprising a seventh compartment containing lactic acid.

96. The container of claim 93, wherein the container has a readable indicia thereon, configured to be recognized by the dialysis treatment unit.

97. The container of claim 93, wherein the compartments contain sufficient quantities of respective contents to enable the container to fill one of a plurality of patient prescriptions.

98. A container for use with a dialysis system, comprising:

a plurality of compartments, at least one of the compartments containing an ionic component of a dialysis solution and another of the compartments containing at least one of a cleaning agent for use in cleaning a flow path in the dialysis system and a precursor of the cleaning agent; and

a plurality of ports on the container for placing the compartments in fluid communication with the dialysis system.

99. The container of claim 98, wherein the compartments include at least a first compartment containing calcium chloride, a second compartment containing magnesium chloride, a third compartment containing sodium chloride, a fourth compartment containing the cleaning agent, a fifth compartment containing sodium bicarbonate, and a sixth compartment containing glucose.

100. The container of claim 99, wherein the compartments further include a seventh compartment containing lactic acid.

101. A container for use with a dialysis system, the container comprising:

a plurality of compartments each containing a chemical composition for use in a dialysis treatment; and

a plurality of ports each being in fluid communication with a respective one of the compartments for placing the compartments in fluid communication with the dialysis system, at least one of the ports being positioned along a surface of

the container so that the at least one port is asymmetric with respect to a longitudinal axis of the surface of the container.

102. The container of claim 101, wherein axes of the ports are aligned.

103. The container of claim 101, further comprising a respective septum on each of the ports, the septum being configured to be pierced by a respective connector on the dialysis system.

104. The container of claim 101, wherein at least some of the ports include a flange capable of engaging a mount on the dialysis system.

105. The container of claim 101, wherein free ends of the ports are coplanar.

106. The container of claim 101, wherein the plurality of compartments include at least a first compartment containing calcium chloride, a second compartment containing magnesium chloride, a third compartment containing sodium chloride, a fourth compartment containing a cleaning agent, a fifth compartment containing sodium bicarbonate, and a sixth compartment containing glucose.

107. The container of claim 106, wherein the compartments further include a seventh compartment containing lactic acid.

108. The container of claim 101, wherein an exterior surface of the container includes a bar code symbol configured to be read by a bar code reader on the dialysis system.

109. The container of claim 101, wherein at least some of the compartments include a respective vent tube.

110. The container of claim 101, wherein at least some of the ports include a first flow path for passing air into a

respective one of the compartments and a second flow path for passing liquid into and removing solution from the respective one of the compartments.

111. A container for use with a dialysis system, comprising:

a plurality of compartments each containing a chemical composition for use in a dialysis treatment;

a plurality of ports for placing the compartments in fluid communication with the dialysis system; and

a readable indicia on the container, the readable indicia being configured to be recognized by the dialysis system, the indicia being indicative of the contents of the compartments.

112. The container of claim 111, wherein the readable indicia is a bar code symbol.

113. The container of claim 111, wherein the readable indicia includes information regarding the contents of the compartments.

114. The container of claim 111, wherein the readable indicia includes patient prescription information..

115. The container of claim 111, wherein the compartments include at least a first compartment containing calcium chloride, a second compartment containing magnesium chloride, a third compartment containing sodium chloride, a fourth compartment containing a cleaning agent, a fifth compartment containing sodium bicarbonate, and a sixth compartment containing glucose.

116. The container of claim 115, wherein the compartments further include a seventh compartment containing lactic acid.

117. A method of making a container for use with a dialysis system, comprising:

providing a container including at least first, second, third, fourth, and fifth compartments, the container further

including a plurality of ports each being in fluid communication with a respective one of the compartments;

placing calcium chloride in the first compartment;

placing magnesium chloride in the second compartment;

placing sodium chloride in the third compartment;

placing sodium bicarbonate in the fourth compartment; and

placing glucose in the fifth compartment.

118. The method of claim 117, wherein the container further includes a sixth compartment, and wherein the method further comprises placing lactic acid in the sixth compartment.

119. The method of claim 117, wherein the container further includes a sixth compartment, and wherein the method further comprises placing a cleaning agent in the sixth compartment.

120. The method of claim 117, further comprising sealing the compartments.

121. The method of claim 117, wherein each of the compartments includes an upper portion and a lower portion, and wherein the sealing includes joining the upper portion and lower portion together.

122. The method of claim 117, further comprising providing a septum in each of the ports.

123. The method of claim 117, further comprising providing a bar code symbol on the container.

124. The method of claim 117, further comprising placing a removable cover on open ends of the ports.

125. A method of making dialysis solution for use during a dialysis treatment session for a patient, comprising:

providing a plurality of compartments containing quantities of differing chemical compositions;

adding liquid to the compartments to form constituents of

dialysis solution in the compartments;

forming from the constituent components a quantity of dialysis solution sufficient to complete the dialysis treatment session without using a portion of at least one of the constituents; and

disposing of the unused portion of the at least one constituent.

126. A method of forming dialysis solution on site at a patient treatment location, comprising:

adding liquid to compartments containing a plurality of different chemical compositions to form chemical component solutions for use in forming dialysis solution;

flowing the chemical component solutions to a mixing chamber;

monitoring at least one of the chemical component solutions flowing to the mixing chamber; and

controlling flow to the mixing chamber of the at least one chemical component solution based on the monitoring.

127. A method of forming dialysis solution at a patient treatment site, comprising:

adding liquid to a plurality of differing chemical compositions to form a plurality of differing chemical component solutions, wherein the chemical compositions include glucose in dry form and the chemical component solutions include glucose solution;

forming in a mixing module dialysis fluid including a mixture of the chemical component solutions; and

placing the mixing module in fluid communication with a patient dialysate line to permit flow of the dialysis solution from the mixing chamber to the patient dialysate line.

128. A method of making dialysis solution at a patient treatment location, comprising:

providing at a patient treatment location components of dialysis solution, at least some of the components being in substantially dry form;

priming at the patient treatment location the substantially dry components of the dialysis solution to form solution components of the dialysis solution;

mixing at least a portion of the solution components together to form a concentrated solution; and

diluting the concentrated solution with liquid to form dialysis solution.

129. A method of performing a dialysis treatment, comprising:

adding liquid to a plurality of differing chemical compositions to form chemical component solutions for use in forming dialysis solution;

mixing at least a portion of the chemical component solutions together in a mixing module to form a concentrated solution;

diluting the concentrated solution with liquid to form dialysis solution in the mixing module; and

flowing the dialysis solution from the mixing module to a patient dialysate line.

130. A method of dialysis treatment, comprising:

connecting a patient dialysate tube to a connector on a dialysis treatment system;

flowing dialysis solution along a flow path in the dialysis treatment system and to the patient dialysate tube;

sterilizing the dialysis solution flowing to the patient dialysate tube at a sterilization module in the system; and

sterilizing at least a substantial portion of the flow path in the dialysis treatment system, wherein the sterilizing of the flow path includes flowing a sterilization liquid in the flow path between the sterilization module and the connector.

131. A dialysis system capable of using tap water to make dialysis solution at a patient treatment location, comprising:

a water treatment module for treating tap water to purify the tap water;

a mixing module flow connected to the water treatment module, for mixing the purified tap water with a plurality of

chemical compositions to form dialysis solution; and

a connector flow connected to the mixing module and being configured to be connected to a patient dialysate line to permit flow of the dialysis solution from the system to the patient dialysate line.

132. A system for forming dialysis solution by priming glucose in substantially dry form on site at a patient treatment location, the system comprising:

a plurality of compartments containing chemical compositions for use in forming dialysis solution, one of the compartments containing glucose in substantially dry form; and

a mixing module for flow connection to the compartments, the mixing module including a plurality of flow paths capable of flow communicating with the compartments, at least one of the flow paths being configured to pass liquid into the compartment containing glucose to thereby form a glucose solution, the mixing module further including a mixing chamber for forming dialysis solution by mixing the glucose solution, the liquid and the contents of the compartments.

133. The system of claim 132, wherein the compartment containing glucose includes a diffuser for facilitating dissolution of the dry glucose in the liquid.

134. A system permitting selective formulation of differing formulations of dialysis solution, the system comprising:

a container including a plurality of compartments containing amounts of chemical components capable of being combined with liquid to form constituents of the dialysis solution;

at least one module including

a plurality of flow paths coupled to the compartments, the flow paths being capable of being flow connected to a source of the liquid to allow for flow of the liquid to the compartments to form the constituents in the compartments,

a mixing chamber in flow communication with the flow

paths to allow for flow of the constituents from the compartments to the mixing chamber, and

at least one flow regulator for regulating flow of the constituents from the compartments to the mixing chamber; and

a controller for controlling the at least one flow regulator to adjust amounts of the constituents flowing to the mixing chamber.

135. A system for forming dialysis solution based on patient information, comprising:

a processor for processing prescription information unique to a dialysis treatment patient;

a mixing module for mixing constituent components of dialysis solution to form dialysis solution;

a controller for controlling the mixing module based on the prescription information so that the mixing module forms a dialysis solution with quantities of the constituent components sufficient for the patient.

136. The system of claim 135, wherein the system further comprises a memory device for storing the prescription information.

137. The system of claim 135, wherein the memory device is a portable device and wherein the system further comprises a reader for reading the prescription information from the memory device.

138. A medical fluid delivery apparatus capable of reducing bacterial growth, comprising:

at least one container connector capable of being placed in flow communication with a container containing at least one substance for delivery to a patient;

a container mounting section including a first portion and a second portion, the first portion being movable with respect to the second portion between a first open position allowing placement of a container in the mounting section and a

second closed position forming a cavity containing the container connector;

a first module in flow communication with the cavity for providing at least one of a disinfecting fluid and a sterilizing fluid to the cavity to reduce microbial growth on the connector; and

a second module in fluid communication with the connector for delivering the substance to a patient.

139. A method of peritoneal dialysis treatment using dialysis fluid produced at a patient treatment location, comprising:

providing a dialysis apparatus including a plurality of compartments each containing a differing component of dialysis fluid, at least one of the components being in substantially dry form;

combining, at the patient treatment location, liquid and at least some of the components to produce component solutions;

forming, at the patient treatment location, dialysis fluid in the apparatus,

wherein the forming of dialysis fluid includes mixing the component solutions:

placing the dialysis apparatus in flow communication with the peritoneal cavity of a patient;

flowing the dialysis fluid into the peritoneal cavity; and

draining the dialysis fluid from the peritoneal cavity.

140. The method of claim 139, wherein said at least one component in substantially dry form includes an osmotic agent.

141. The method of claim 140, wherein the osmotic agent is glucose.

142. The method of claim 139, further comprising flowing tap water to the apparatus and purifying the tap water to produce purified water, wherein the liquid includes at least the purified tap water.

143. The method of claim 139, further comprising sterilizing at

least one of the liquid and the dialysis fluid in the apparatus.

144. The method of claim 139, wherein the dialysis apparatus includes a processing machine and a removable container in which the plurality of components are located, and wherein the method includes flow connecting the container to the processing machine at a beginning of a treatment session and removing the container from the processing machine at an end of the treatment session.

145. The method of claim 139, wherein the forming of dialysis fluid includes sensing concentration of chemical compositions in the component solutions and regulating flow of the component solutions to a mixing chamber based on the sensing.

146. A method of peritoneal dialysis treatment using dialysis solution formulated at a patient treatment location according to a predetermined formulation, the method comprising:

providing a processing machine configured to form, at a patient treatment location, dialysis solution from components thereof;

engaging with the processing machine a container containing the components of dialysis solution, the container containing a quantity of components sufficient to form one of a plurality of differing formulations of dialysis solution;

processing in the machine, information about a predetermined patient prescription;

forming a predetermined formulation of dialysis solution in the machine according to the patient prescription;

placing the apparatus in flow communication with the peritoneal cavity of the patient;

flowing the dialysis solution into the peritoneal cavity;

removing the dialysis solution from the peritoneal cavity; and

disengaging the container from the processing machine.

147. The method of claim 146, further comprising inputting of

prescription information, the inputting including at least one of reading information from a smart card, receiving information via a modem, and manually entering information on a user interface.

148. The method of claim 147, wherein the inputting of information includes: inputting a desired osmotic substance concentration, and wherein the forming of the predetermined formulation includes formulating the dialysis solution with approximately the desired osmotic substance concentration.

149. The method of claim 146, wherein the forming of the predetermined formulation of dialysis solution includes

adding liquid to differing chemical compositions;

processing in the machine, information about a predetermined patient prescription;

forming a predetermined formulation of dialysis solution in the machine according to the patient prescription;

placing the apparatus in flow communication with the peritoneal cavity of the patient;

flowing the dialysis solution into the peritoneal cavity;

removing the dialysis solution from the peritoneal cavity; and

disengaging the container from the processing machine.

150. The method of claim 146, wherein the forming of the predetermined formulation of dialysis solution includes adding liquid to differing chemical compositions to form differing chemical component solutions, and mixing quantities of the chemical component solutions.

151. The method of claim 150, wherein at least some of the chemical compositions are in substantially dry form.

152. A container for use with a dialysis system, the container comprising:

a first compartment including a first air vent channel and a first fluid channel;

a second compartment including a second air vent channel and a second fluid channel;

a third compartment including a third air vent channel and a third fluid channel;

a fourth compartment including a fourth air vent channel, a fluid input channel, a diffuser in flow communication with the fluid input channel, a fluid output channel, and a glucose filter in flow communication with the fluid output channel;

a fifth compartment including a fifth air vent channel and a liquid channel;

a sixth compartment including a first air vent/fluid flow channel and a first fluid input/output channel;

a seventh compartment including a second air vent/fluid flow channel and a second fluid input/output channel;

a first port in flow communication with the first air vent channel and the first fluid channel;

a second port in flow communication with the second air vent channel and the first fluid flow channel;

a third port in flow communication with the third air vent channel and the third fluid channel;

a pair of fourth ports, one of the fourth ports being in flow communication with the fluid input channel and the fluid output channel, the other of the fourth ports being in flow communication with the fourth air vent channel;

a fifth port in flow communication with the fifth air vent channel and the liquid channel;

a sixth port in flow communication with the first air vent/fluid flow channel and the first fluid input/output channel; and

a seventh port in flow communication with a second air vent/fluid flow channel and a second fluid input/output channel,

wherein a plurality of the compartments are sized to contain respective amounts of dialysis solution components capable of filling a plurality of differing dialysis solution prescriptions, and wherein the ports are capable of being placed in flow communication with a dialysis processing machine.

153. The container of claim 152, further comprising:

calcium chloride in the first compartment, capable of being combined with liquid to form a first constituent of dialysis solution;

lactic acid in the second compartment, capable of being combined with liquid to form a second constituent of dialysis solution;

cleaning agent in the third compartment, capable of being combined with liquid to form a cleaning solution;

glucose in the fourth compartment, capable of being combined with liquid to form a third constituent of dialysis solution, the glucose being in substantially dry form;

magnesium chloride in the fifth compartment, capable of being combined with liquid to form a fourth constituent of dialysis solution;

sodium bicarbonate in the sixth compartment, capable of being combined with liquid to form a fifth constituent of dialysis solution; and

sodium chloride in the seventh compartment, capable of being combined with liquid to form a sixth constituent of dialysis solution.

154. The container of claim 152, wherein the first, second, third, fourth, fifth, sixth, and seventh connectors are aligned along an axis offset from a central axis of the container.

155. The container of claim 152, wherein the container includes a lid and a skirt, the first, second, third, fourth, fifth, sixth, and seventh compartments being between the lid and the skirt and the second, third, fourth, fifth, sixth, and seventh connectors extending through holes in the skirt.

156. A dialysis system, comprising:

a water purification module including:

a tap water inlet,

at least one particulate filter in flow communication with the tap water inlet;

a degassing section including a degassing chamber configured to remove gas from the water,

a first reverse osmosis membrane unit having a first inlet, a first purified water outlet, and a first waste water outlet, and

a second reverse osmosis membrane unit having a second inlet, a second purified water outlet, and a second waste water outlet, the first purified water outlet being in flow communication with the second inlet, and the second waste water outlet being in flow communication with the first inlet:

a thermal control and sterilization module in flow communication with the water purification module, the thermal control and sterilization module including a plurality of heat exchangers configured to transfer heat between liquids flowing in the system;

a concentrate mixing module in flow communication with the water purification module and the thermal control and sterilization module, the concentrate mixing module including:

a plurality of flow couplers having flow channels, at least some of the flow couplers being configured to be placed in flow communication with respective compartments containing concentrated components of dialysis solution,

a plurality of valves configured to regulate flow of liquid, the plurality of valves including a respective valve associated with each of the flow couplers to regulate at least one of liquid flow to and liquid flow from the compartments,

a concentrate reservoir in flow communication with the flow couplers, a least one conductivity sensor configured to sense conductivity of liquid flowing to the concentrate reservoir,

a mixing chamber in flow communication with the concentrate reservoir and with a purified water output of the water purification module to permit formation of dialysis solution, and at least one pump in flow communication with the flow couplers, the concentrate reservoir, and the mixing chamber;

an outflow drain; and

a connector configured to be connected to a patient

dialysate line, the connector being in flow communication with the mixing chamber to permit flow of the dialysis solution to the patient dialysate line.

157. The system of claim 156, wherein the flow couplers include spikes adapted to extend into ports on a container.

158. The system of claim 156, wherein the thermal control and sterilization module is configured to heat dialysis fluid flowing from the mixing chamber to the connector to thereby sterilize the dialysis fluid.

Abstract

System

Method, apparatus and components of dialysis systems. The apparatus (100) for the preparation of peritoneal dialysis fluid comprises a water preparation module (200) which purifies tap water and supplies the purified water to a thermal control and sterilisation module (300). The thermal control and sterilisation module (300) passes the purified water to a concentrate mixing module (400), which mixes the purified water with concentrated components of the dialysis fluid from a disposable concentrate container (402) to produce the peritoneal dialysis fluid. At least some of the concentrated components of the dialysis fluid are in powdered form. The peritoneal dialysis fluid is passed from the concentrate mixing module (400) back to the thermal control and sterilisation module (300) where it is sterilised in an on-line autoclave, before being passed to a cycler and sterilisable connector module (600) for administration to the patient (50). The apparatus has the advantage that the peritoneal dialysis fluid is prepared on-line at a treatment location, such as a patient's bedroom, to a prescription specific to the patient.

(Fig. 2)

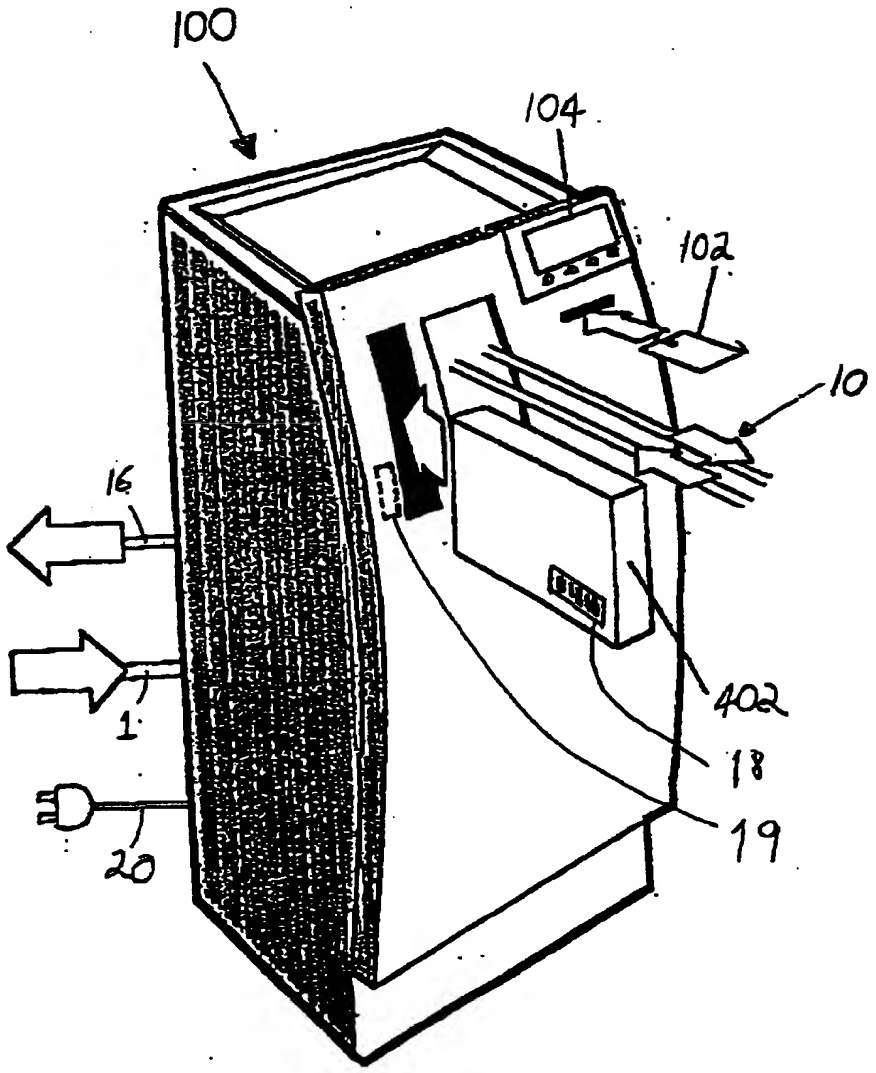

FIG. 1

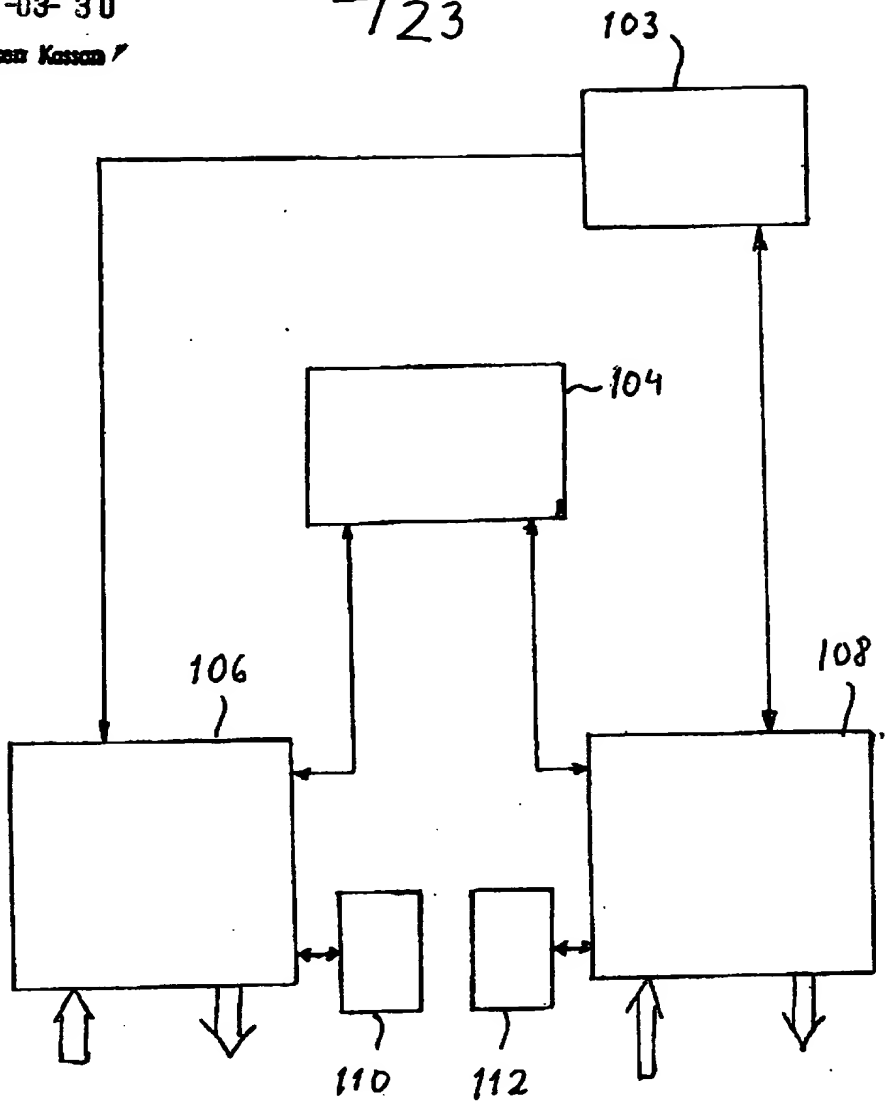

Fig 1a

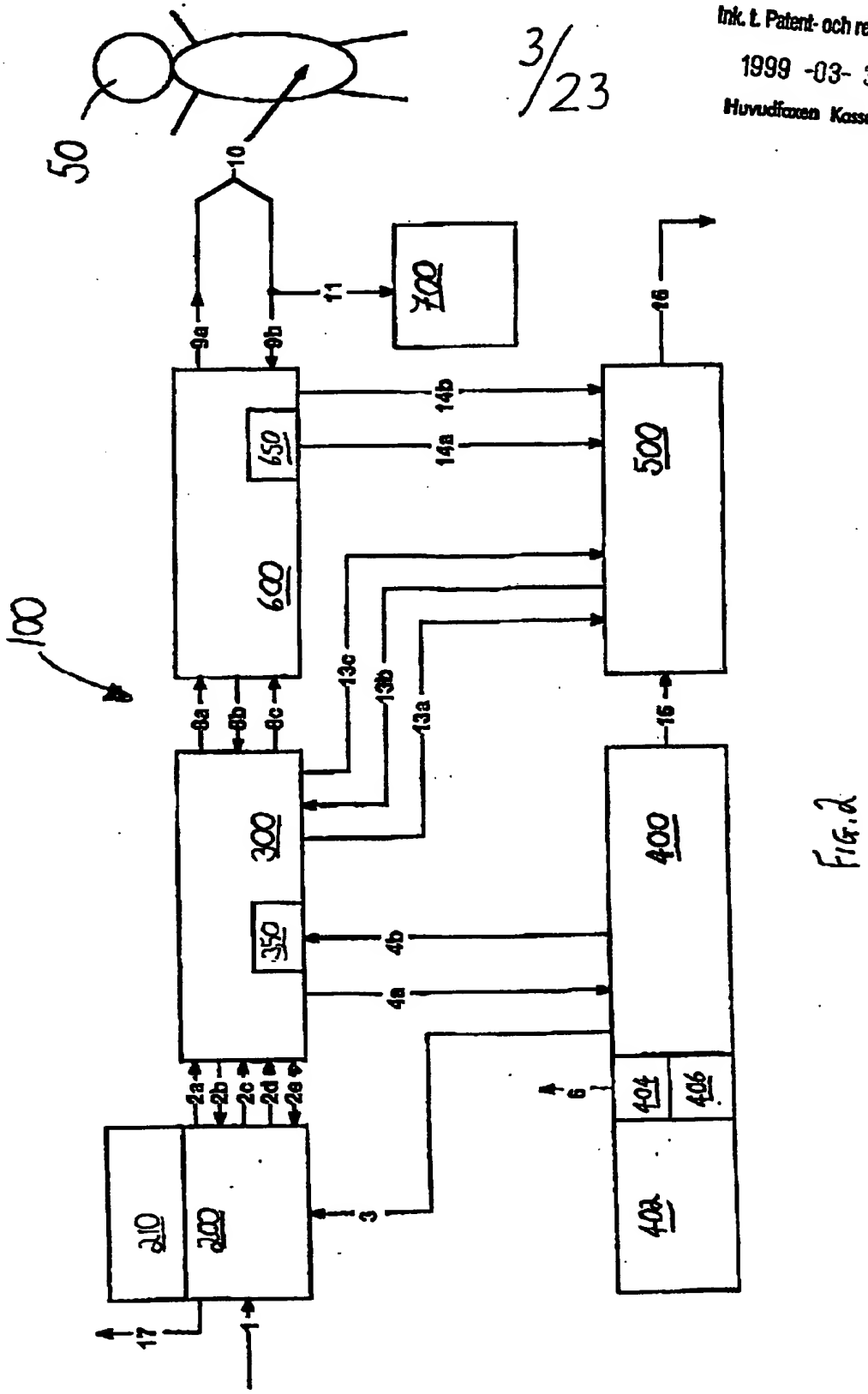

Fig. 2

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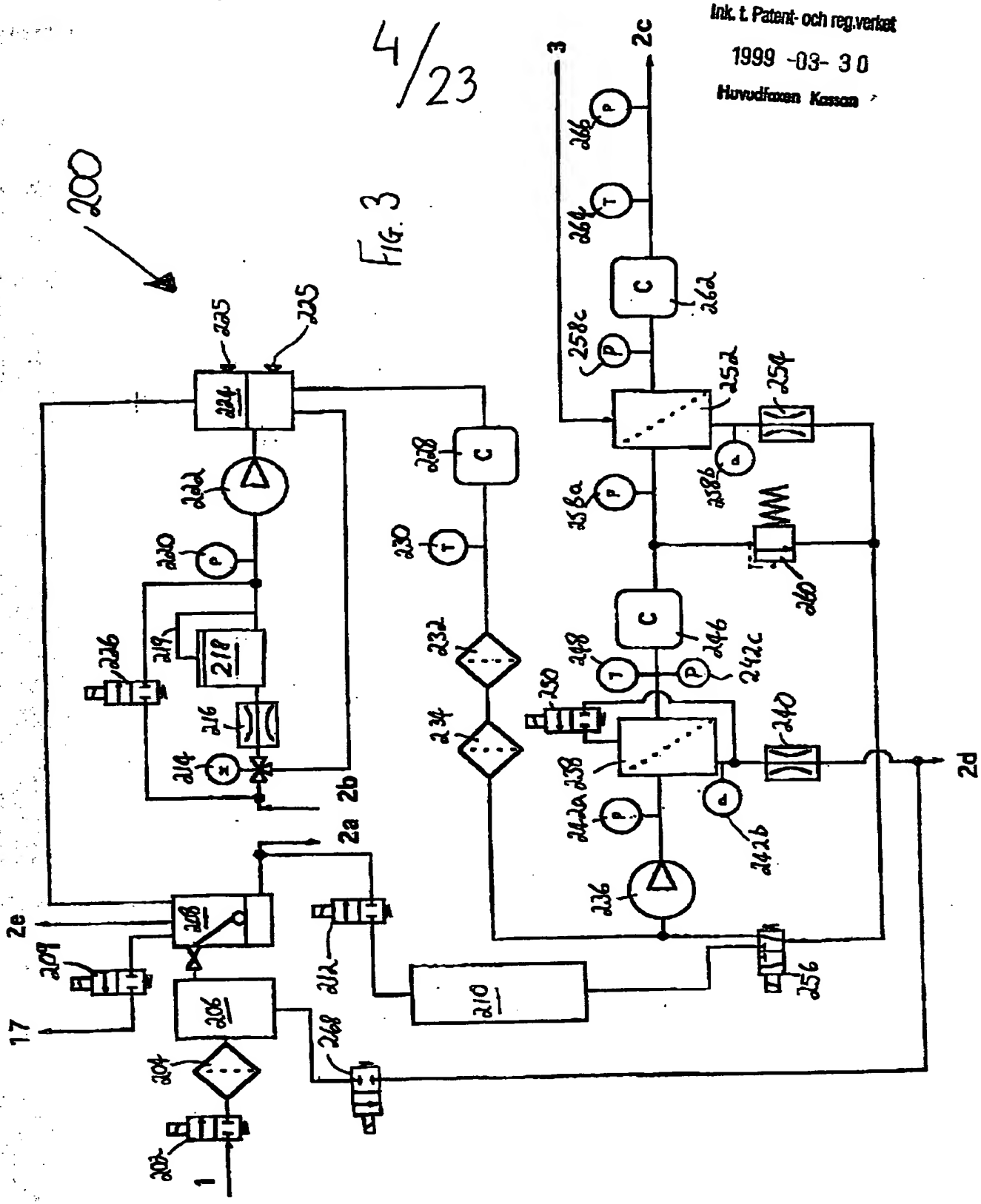
FIG. 3



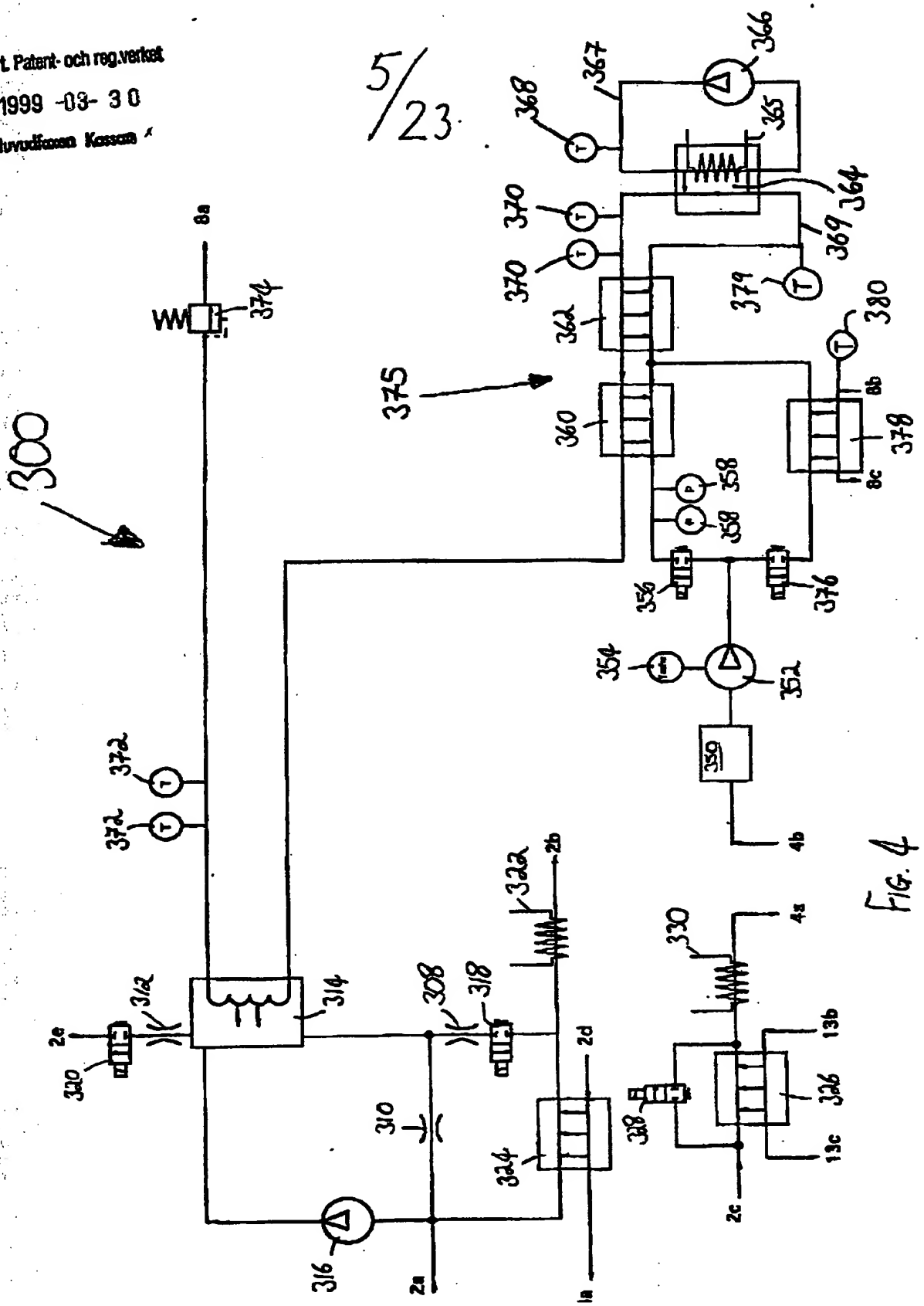


FIG. 4

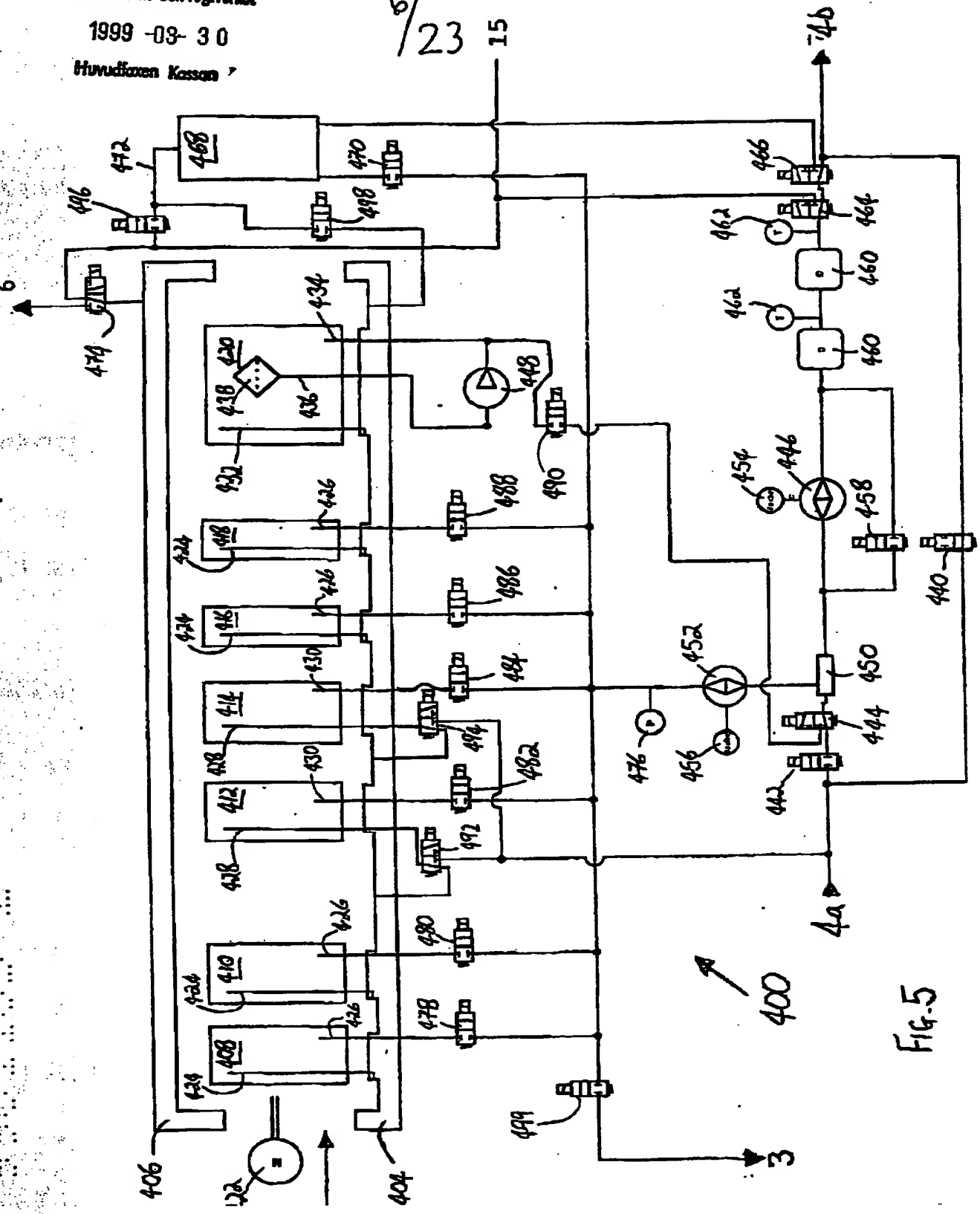


Fig.5

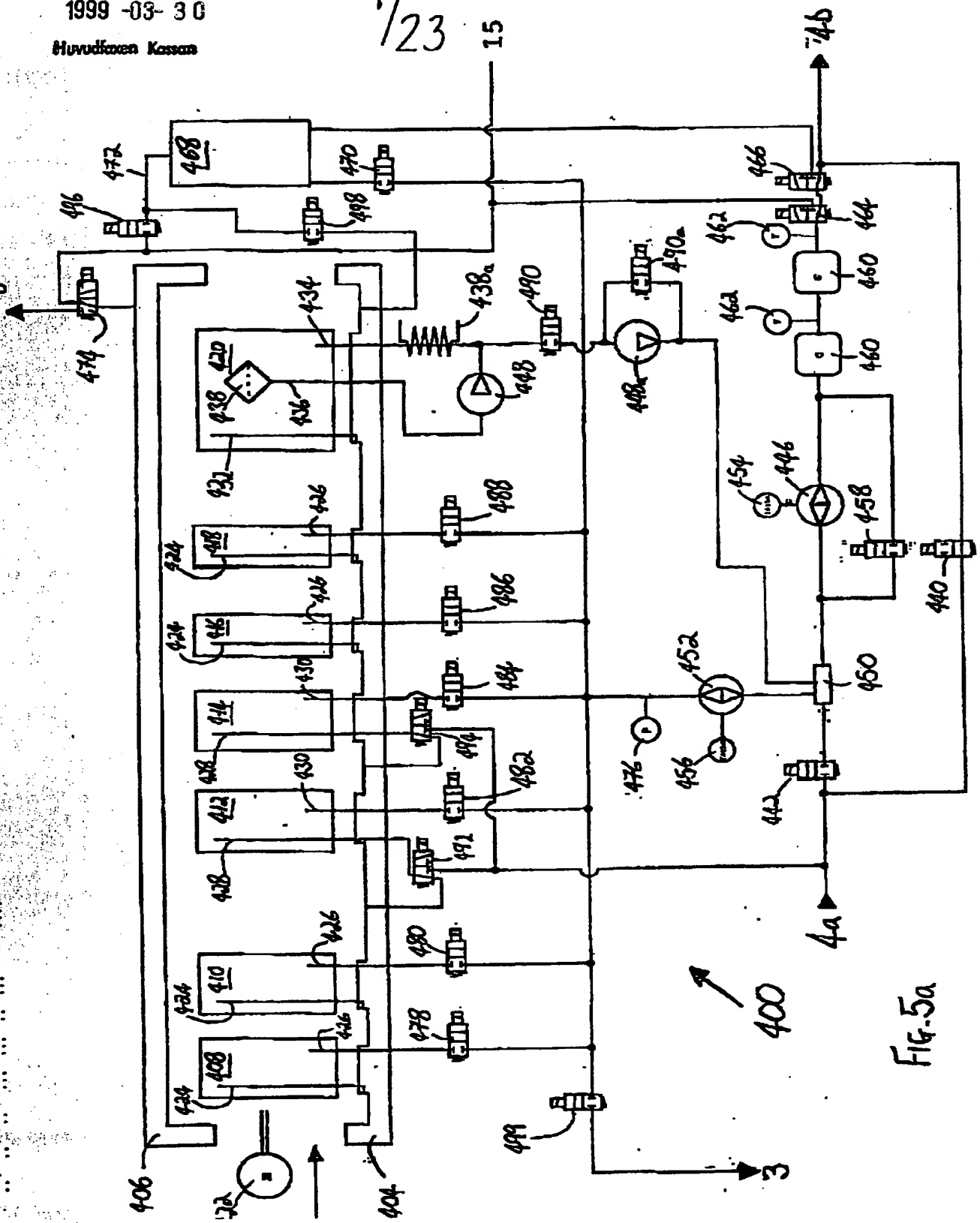


Fig. 5a

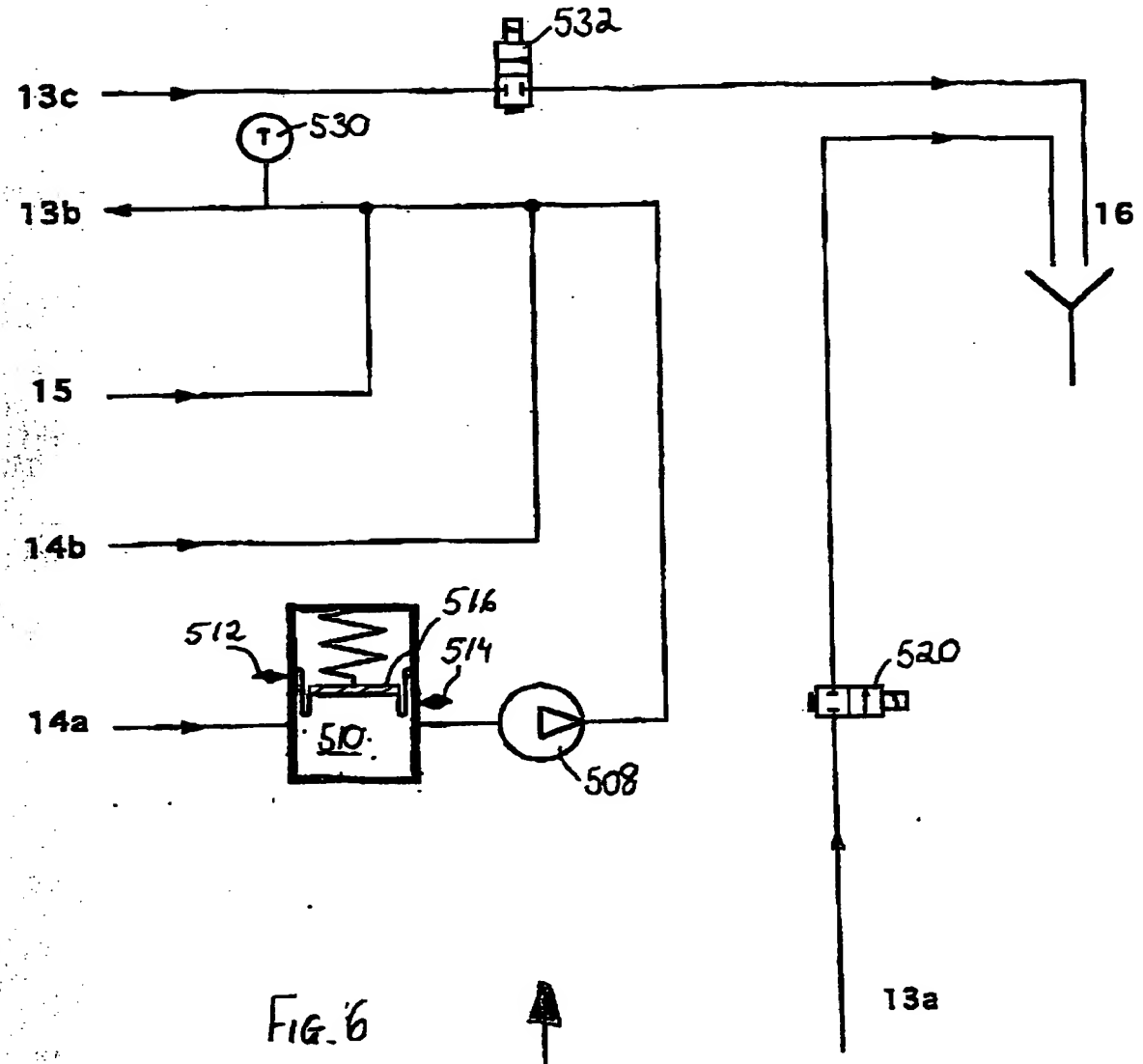


FIG. 6

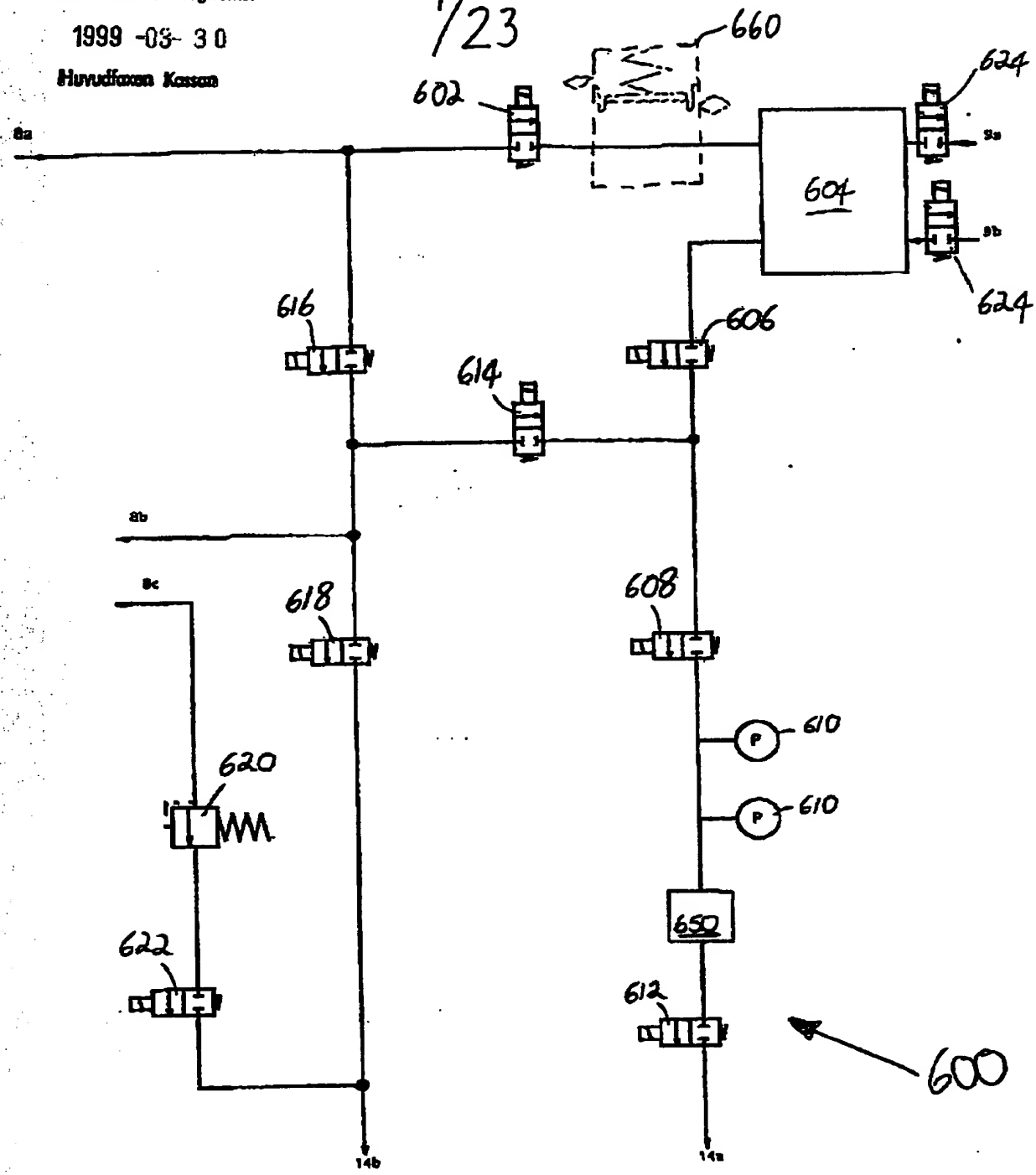


FIG. 7

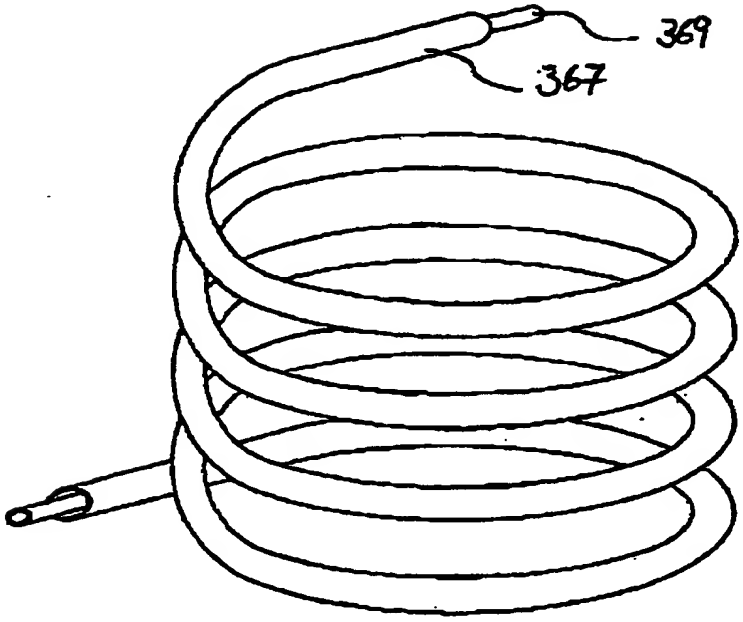


Fig. 8

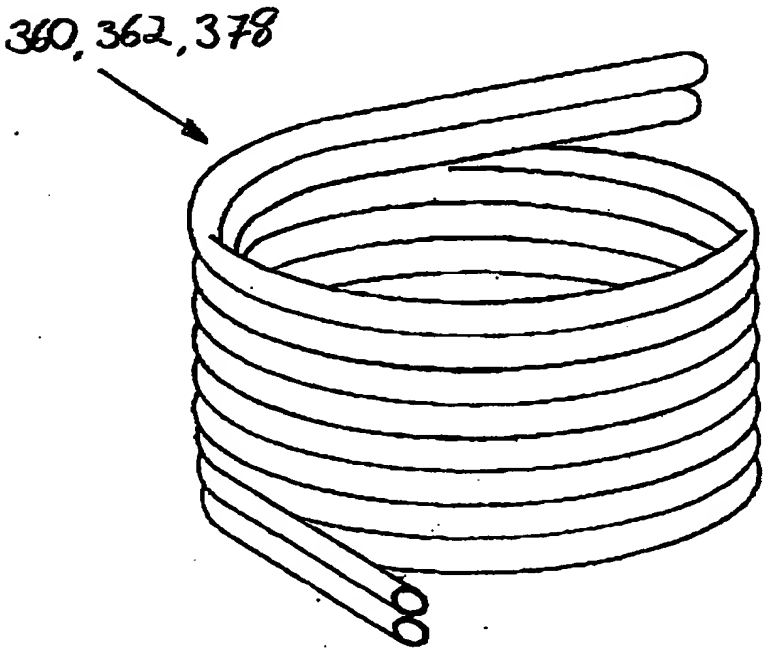


Fig. 9

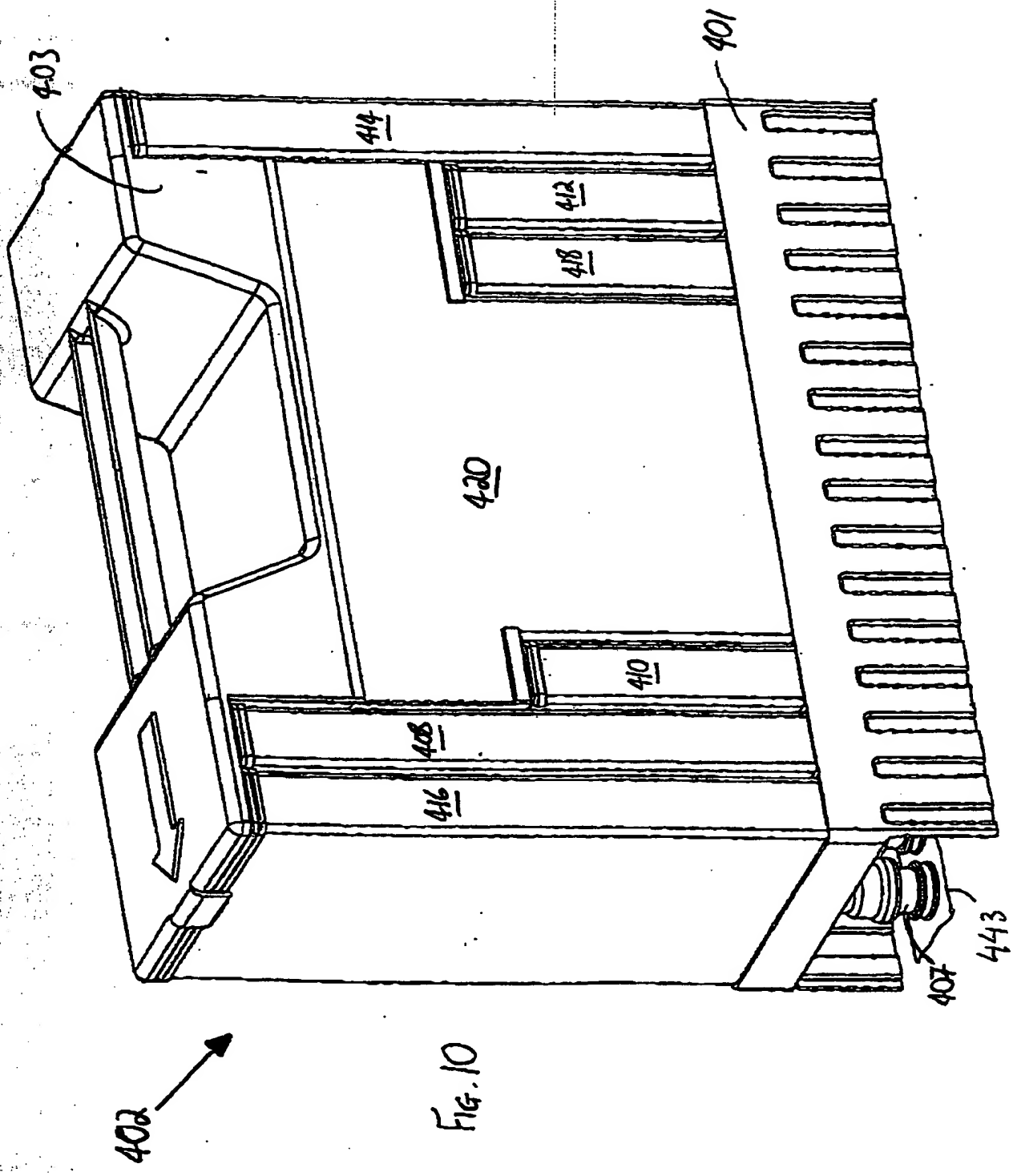


FIG. 10

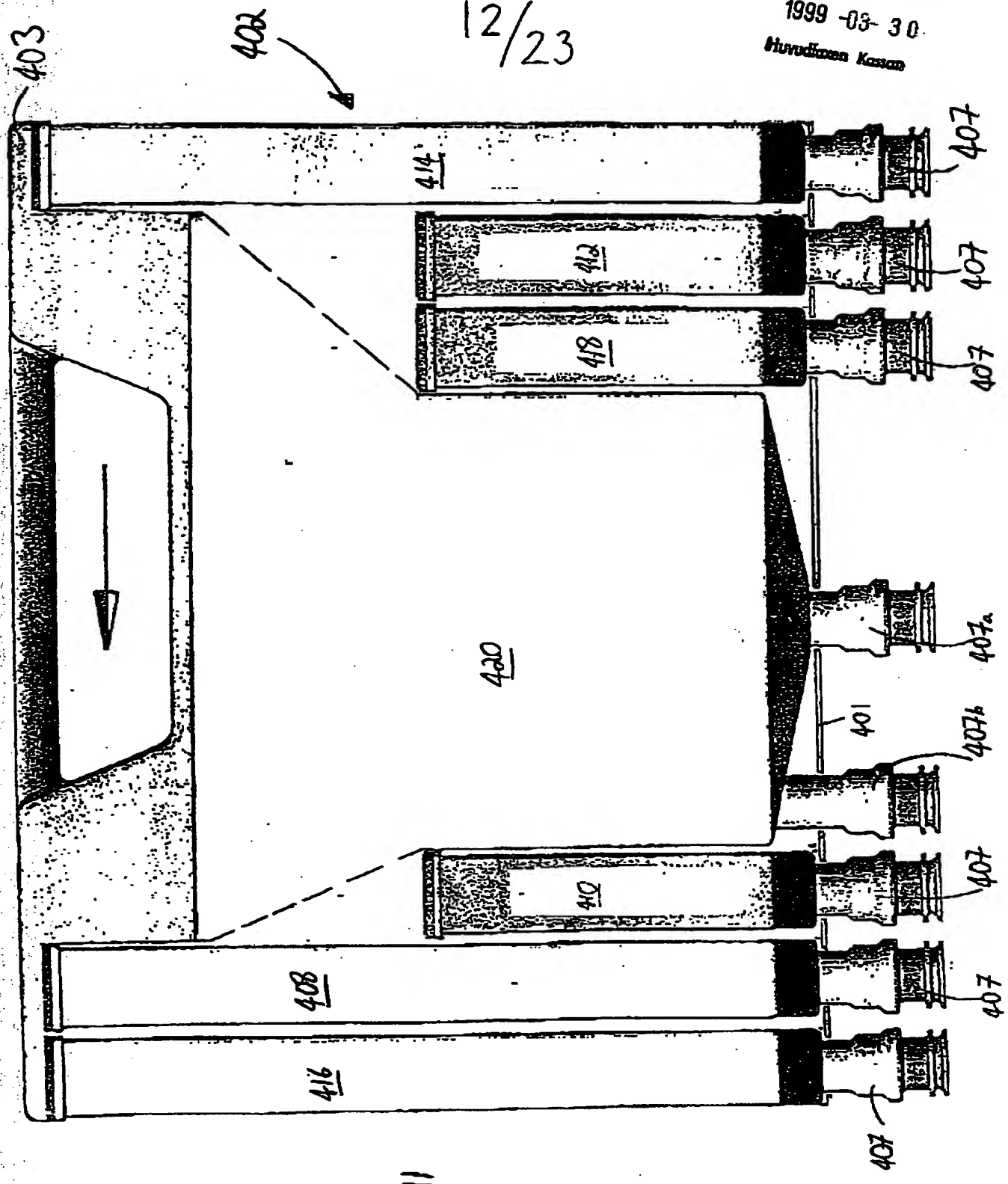


Fig. 11

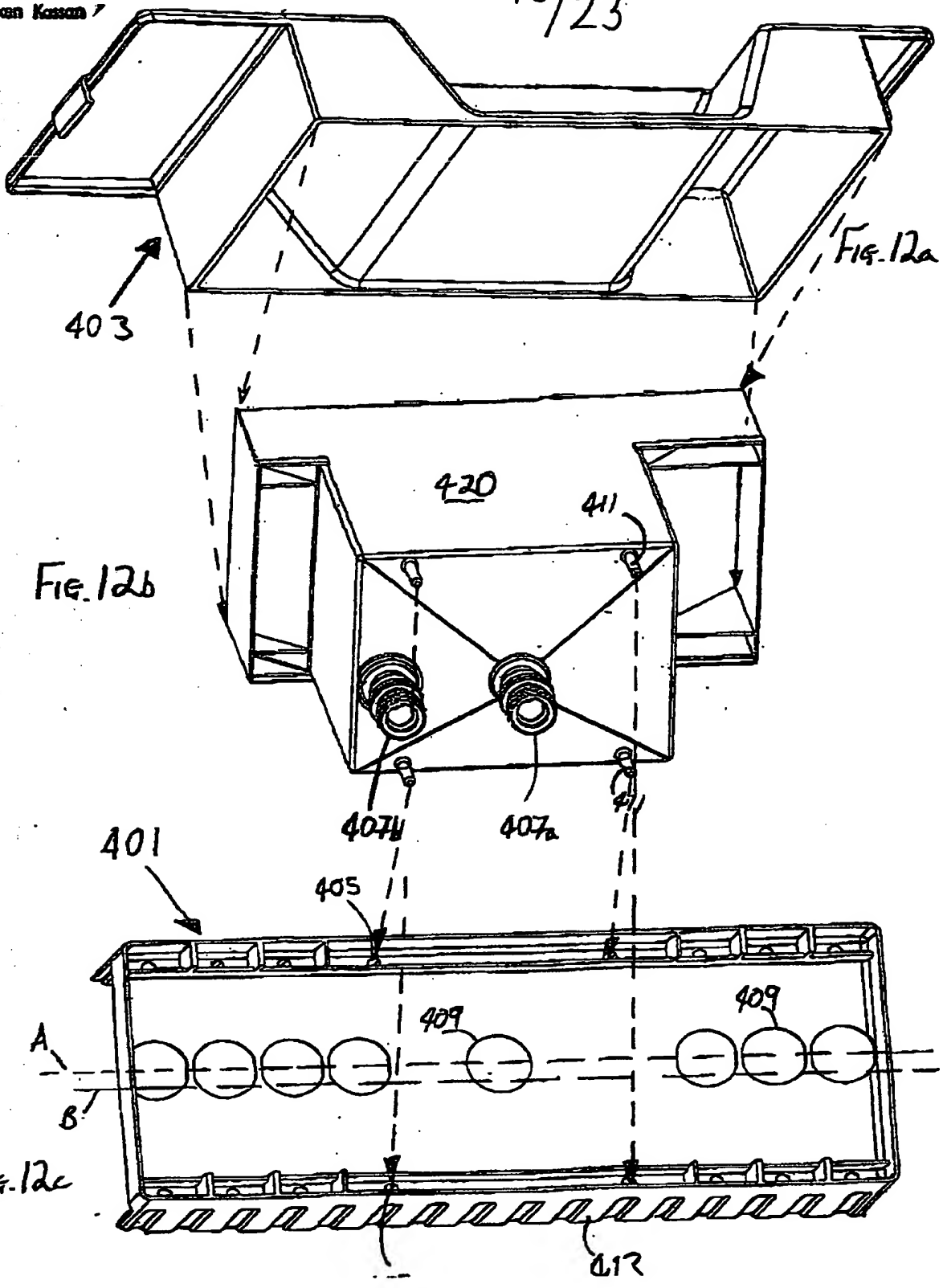


Fig. 12a

Fig. 12b

Fig. 12c

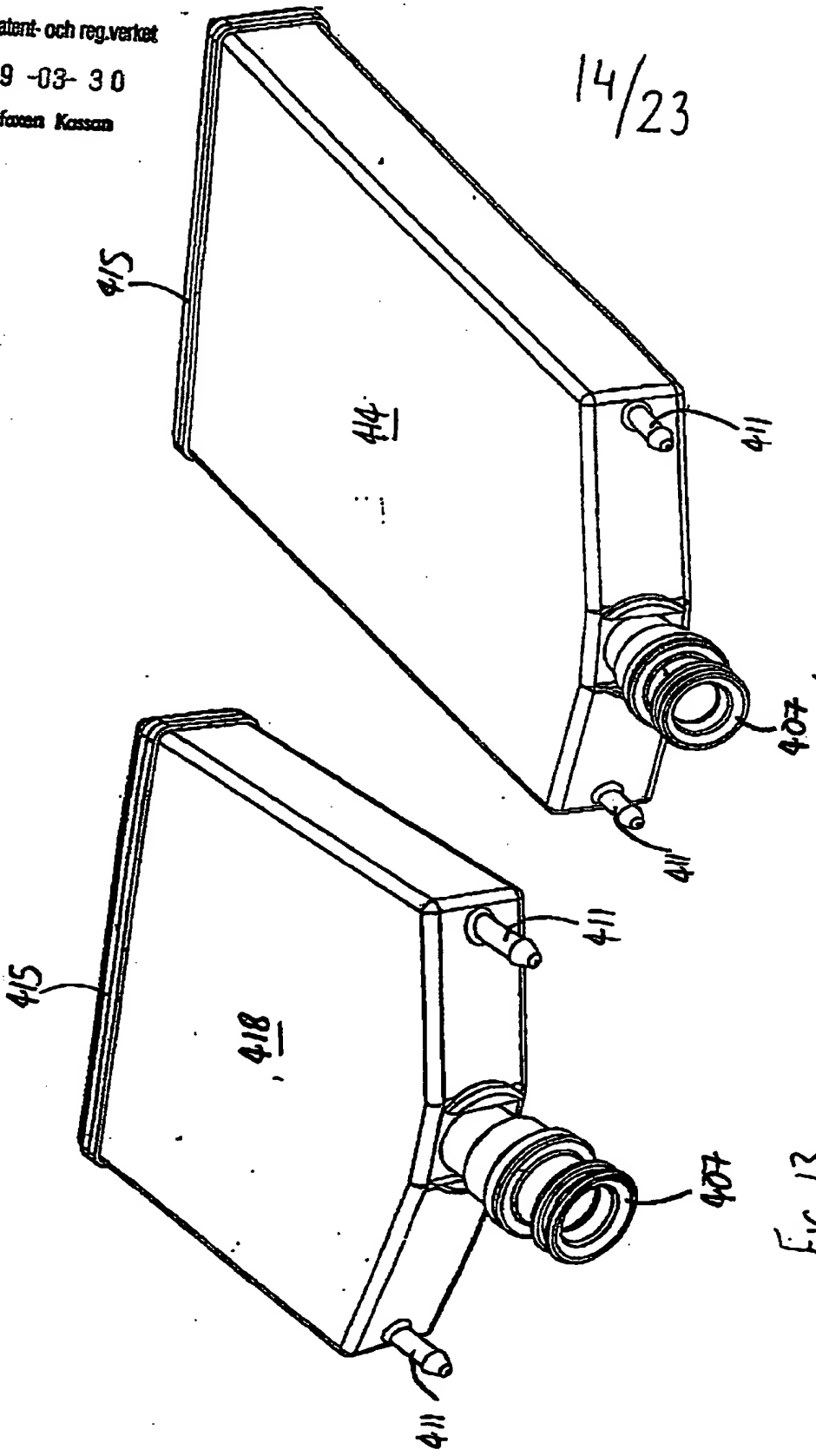


FIG. 14

FIG. 13

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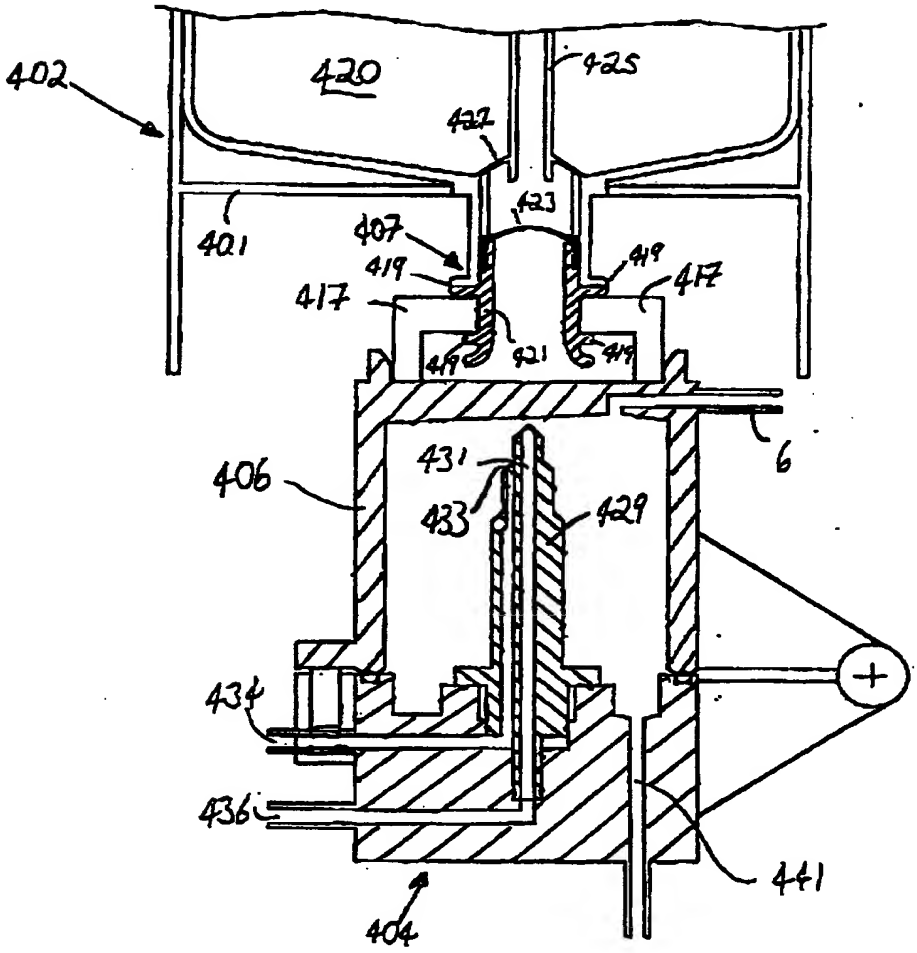


FIG. 15

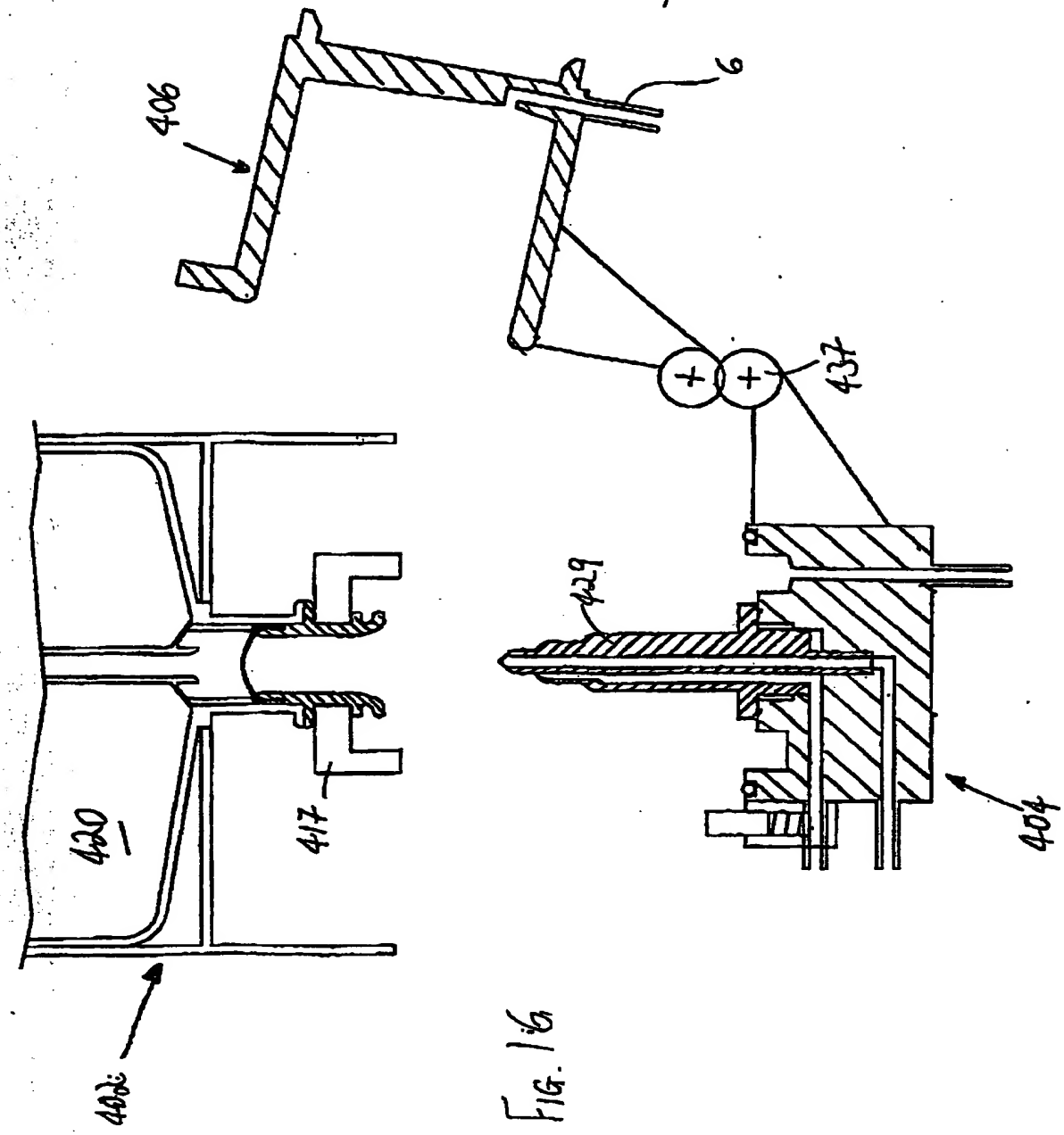


FIG. 16

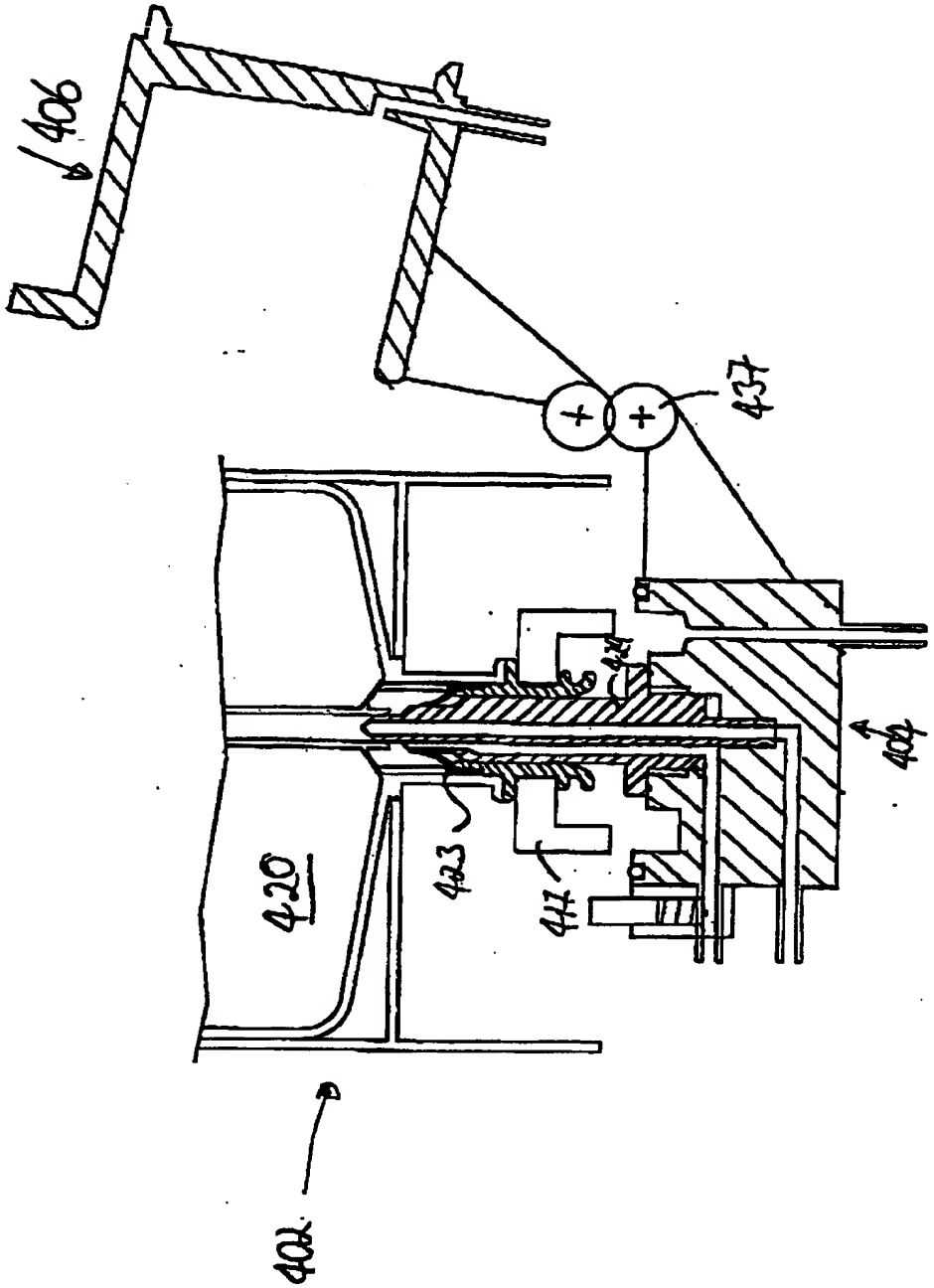


FIG. 17

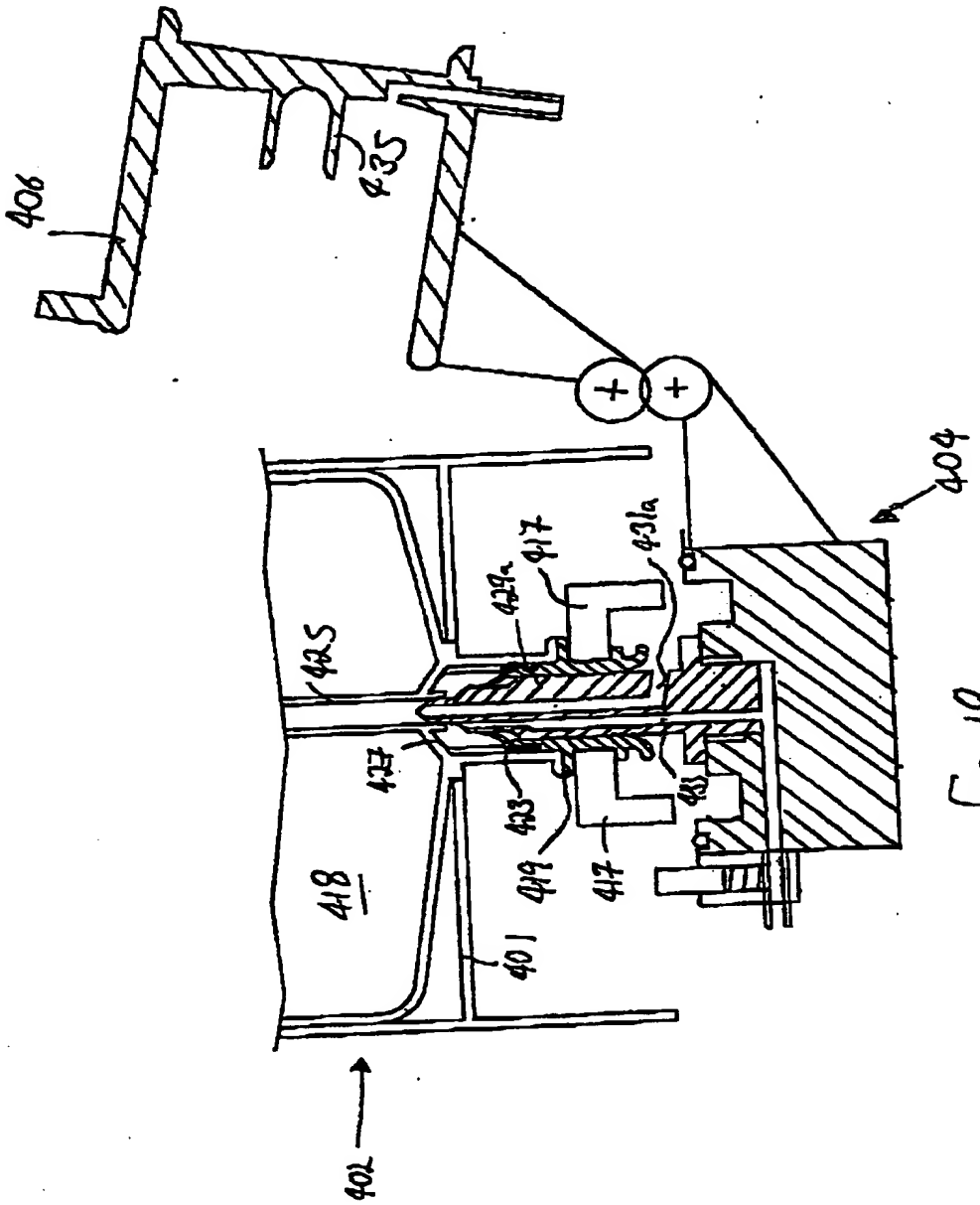


FIG. 18

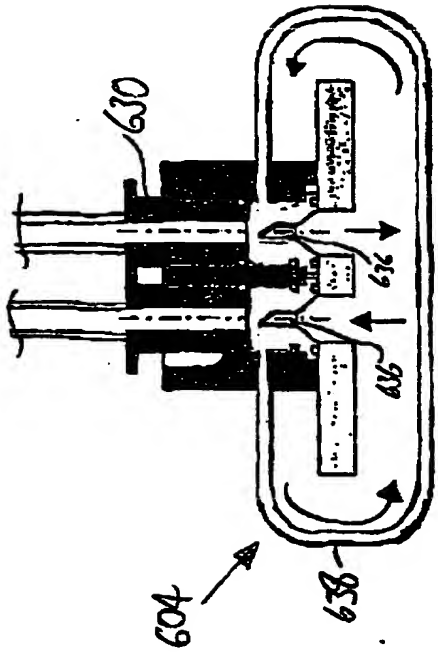


Fig. 19b

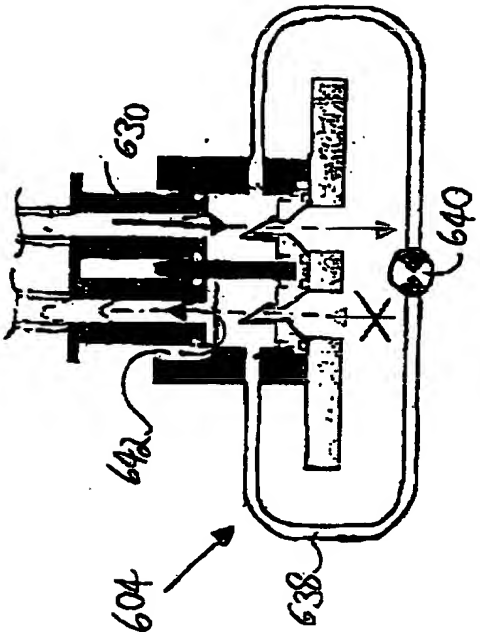


Fig. 19d

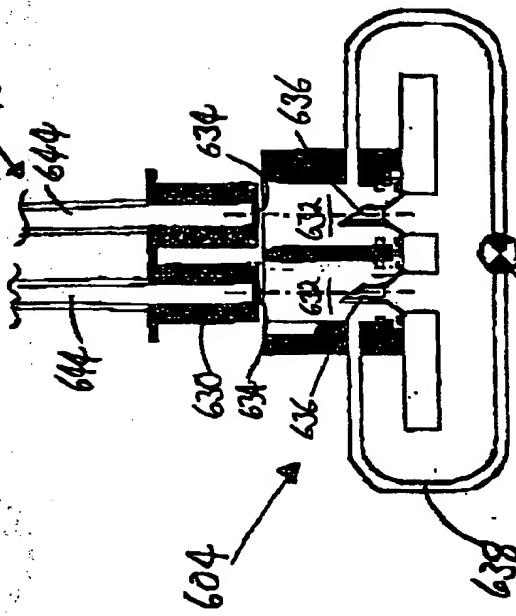


Fig. 19a

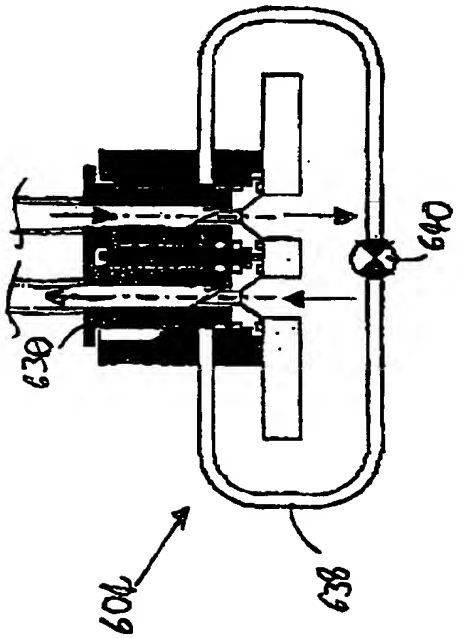


Fig. 19c

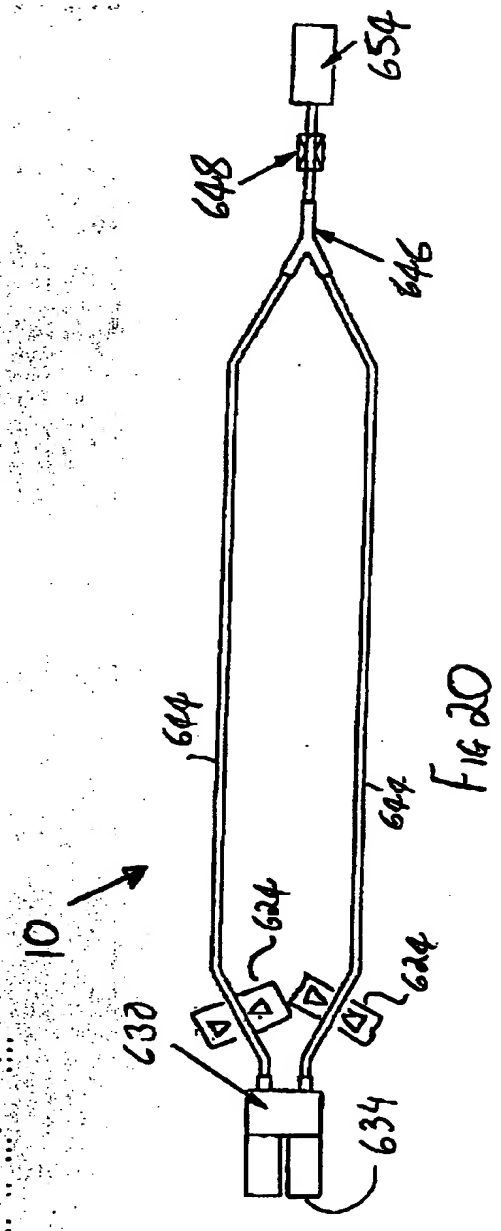


Fig 20

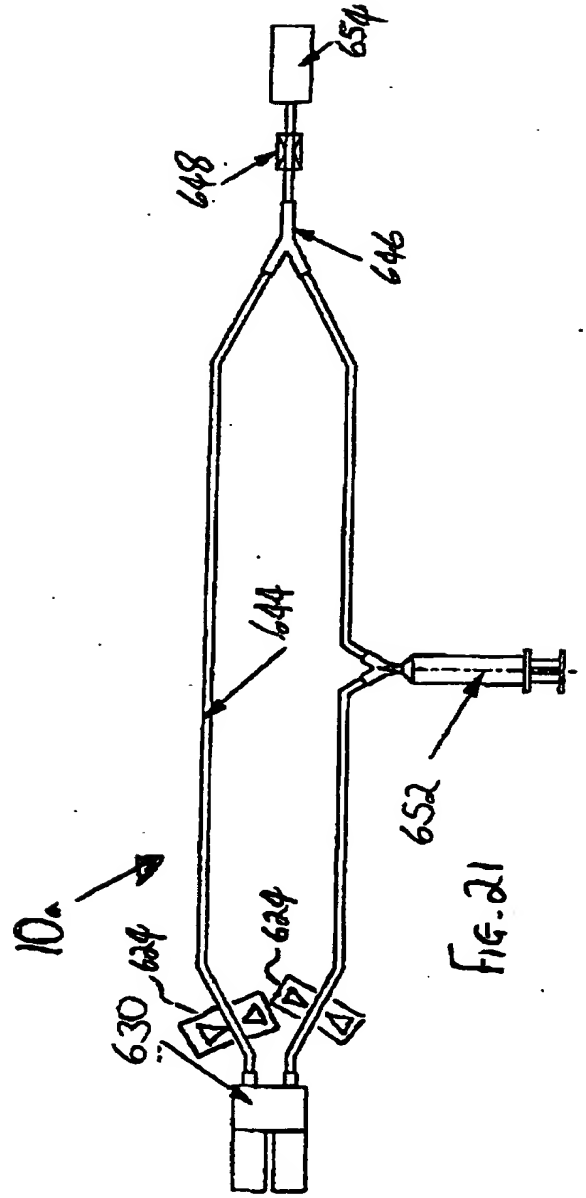


Fig. 21

46 46 169 189

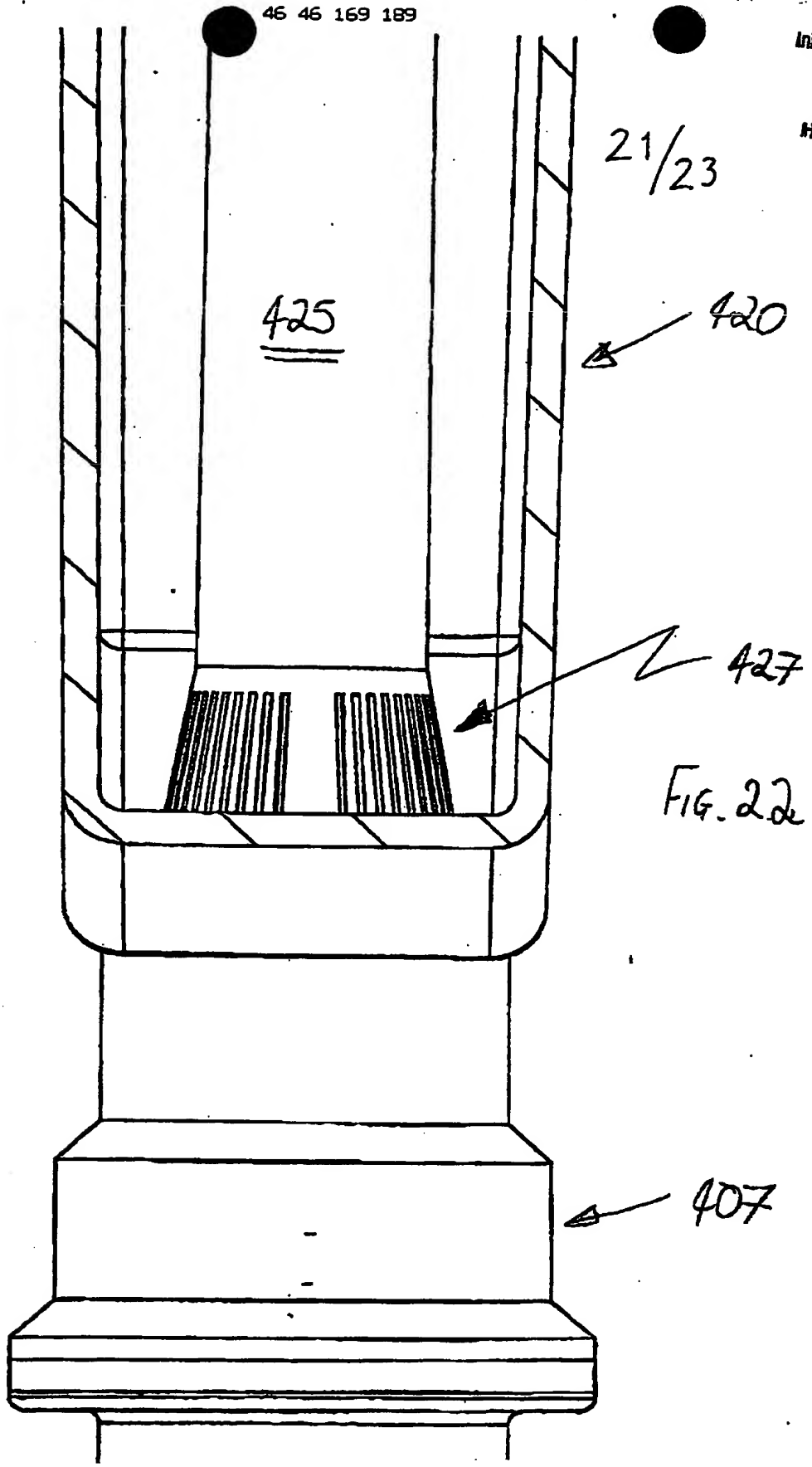
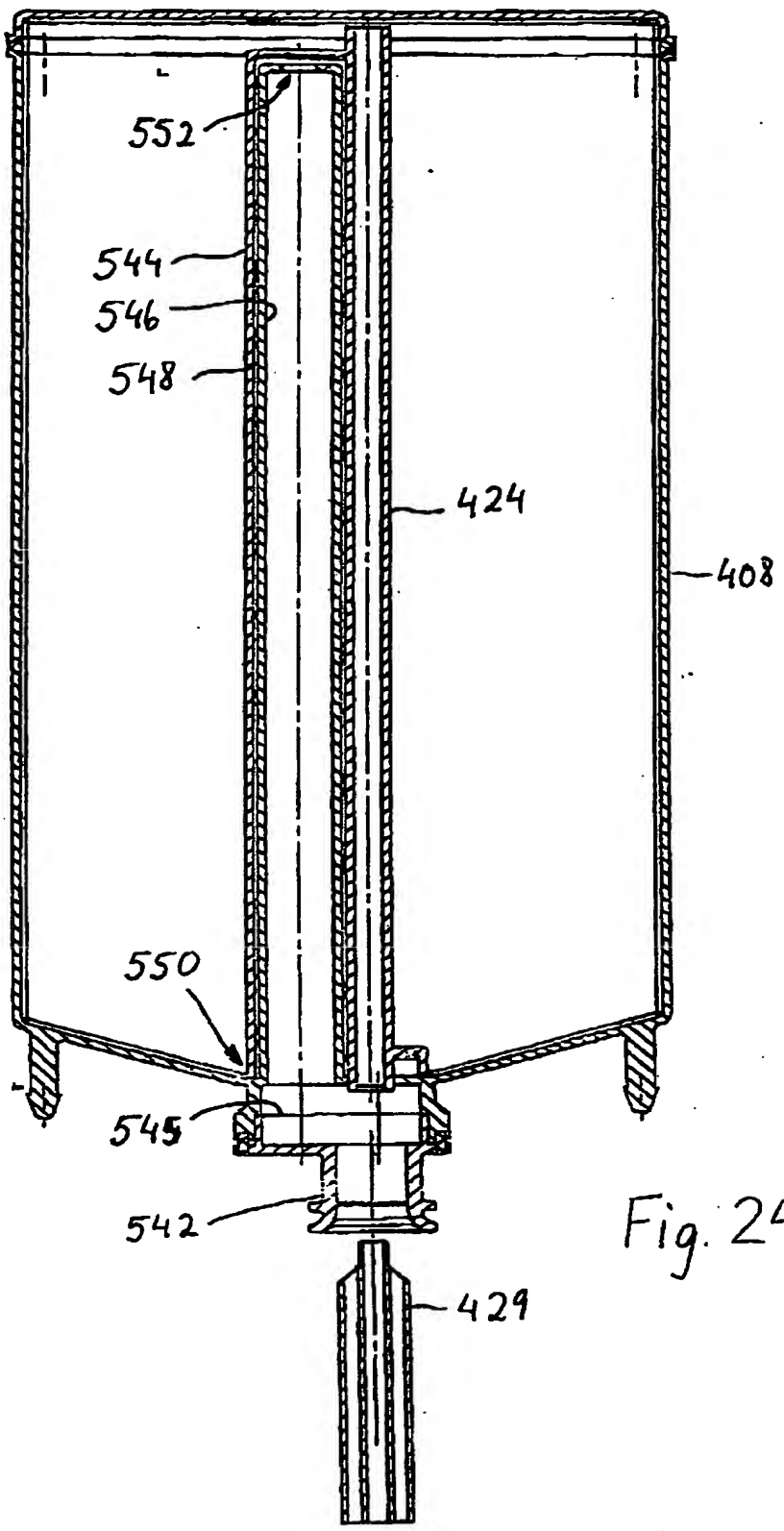
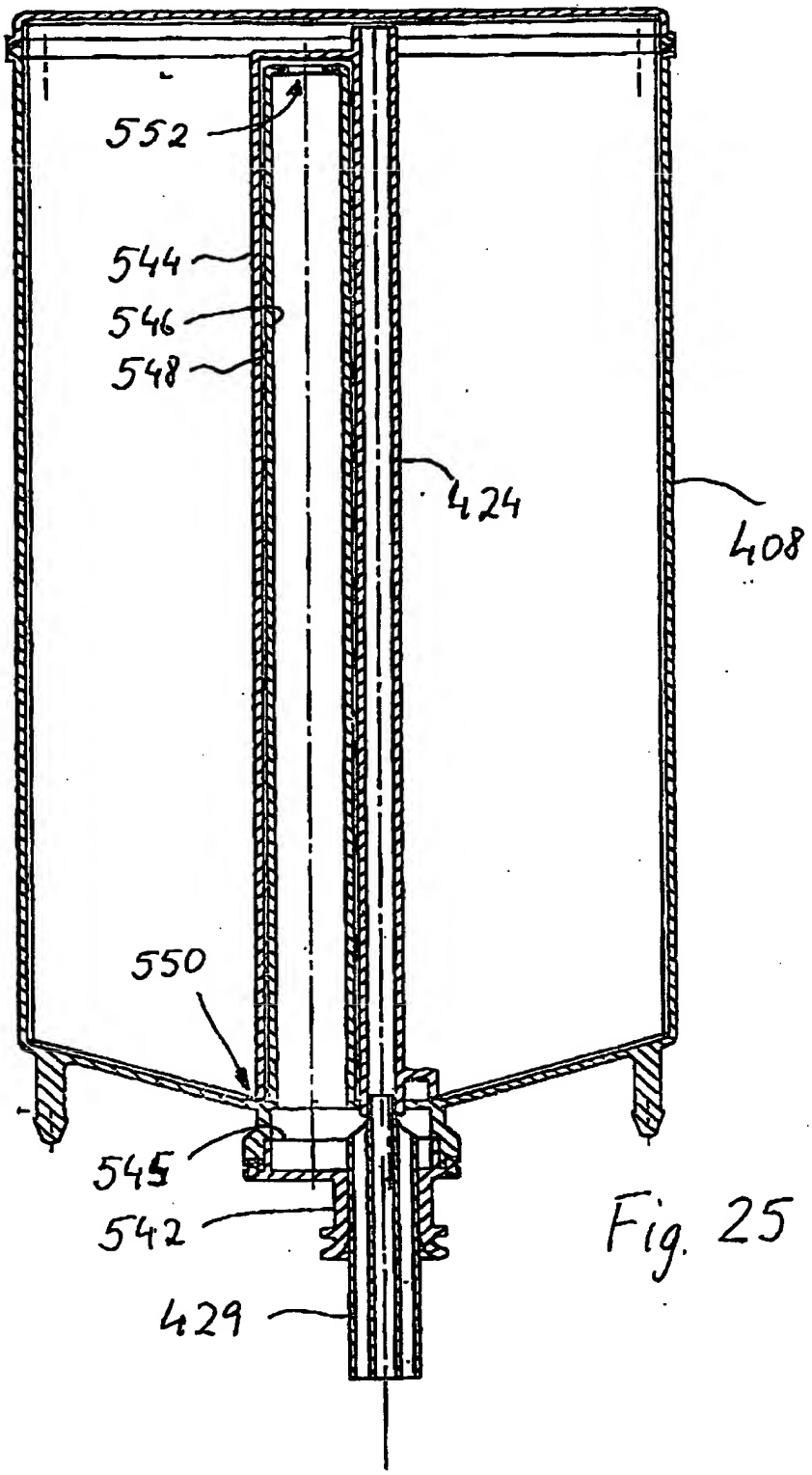


FIG. 22



A-A

Fig. 24



A-A

Fig. 25

Attachment:
Reference HP1310

PROCESS AND DEVICE FOR STERILIZING AND DISPENSING A LIQUID FOR MEDICAL USE

The present invention relates to a process and a device for sterilizing and dispensing a liquid for medical use.

Many surgical and medical treatments exist which require the use of large amounts of sterile liquid, in particular of liquid to be injected into a body cavity or into the bloodstream.

For example, mention may be made of haemofiltration, which is one of the treatments used to overcome renal insufficiency. Haemofiltration consists in extracting, from the blood of a patient, by means of ultrafiltration, a determined amount of plasmatic water and in simultaneously infusing the patient with a smaller amount of a so-called substitution solution, which is sterile and contains the main electrolytes of the blood in respective concentrations which are identical or close to those of the blood of a healthy patient. For a four-hour haemofiltration session, it is not uncommon to prescribe an exchange volume for which about sixteen liters to twenty liters of substitution solution are required.

Another example of a treatment which requires the use of a large amount of sterile liquid is automatic peritoneal dialysis. The principle of peritoneal dialysis, the purpose of which is also to overcome renal insufficiency, is to infuse, into the peritoneal cavity of a patient, a determined amount of a sterile solution containing an osmotic agent such as

glucose as well as the main electrolytes of the blood in respective concentrations similar to those of the blood of a healthy patient. The solution thus infused is left to stand in contact with the peritoneum, which behaves like a natural dialysis membrane, for the time required for the solution to become optimally enriched in blood impurities (urea, creatinine). The waste solution containing added plasmatic water which the glucose has caused to migrate into the peritoneal cavity is then drained from the patient's abdomen and is then replaced with fresh solution.

In the standard method of peritoneal dialysis, known as "continuous ambulatory peritoneal dialysis (CAPD)", it is the patient himself who carries out the operations of draining and filling his peritoneal cavity, by connecting a drain bag or a solution bag to the end of a catheter permanently installed through his abdominal wall. The transfer of liquid from the peritoneal cavity to the collecting bag and from the bag of solution to the peritoneal cavity takes places by gravity, the collecting bag being kept below the level of the abdomen and the bag filled with fresh solution being kept above the level of the abdomen. Typically, a patient carries out the draining-filling operations which have just been described four to five times a day and each exchange involves two liters of liquid.

In the peritoneal dialysis method known as "automatic peritoneal dialysis (APD)", the draining-filling operations are carried out overnight, while the patient is resting, using a machine essentially comprising a pump for circulating the drain liquid and the fresh dialysis solution, a heating device

for heating the fresh solution, a balance for weighing the bags of fresh solution and of drain liquid and for measuring the weight loss, and a programmable control unit for controlling the alternation of the cycles of dwelling and of draining-filling. Since this mode of treatment is administered by a machine and while the patient is resting, it allows a larger number of exchanges than in standard peritoneal dialysis: five or ten exchanges are usually carried out per night, requiring from ten to thirty liters of fresh solution.

In general, the sterile liquids used for carrying out medical treatments of the type which have just been mentioned are prepared industrially and are packaged in flexible plastic bags. Besides the fact that it is unsuitable for the production of unstable solutions (sodium bicarbonate), this preparation method has several drawbacks, in particular the cost of transporting and storing heavy and bulky bags of solutions and the need to manage products which have expiry dates. To overcome these drawbacks, devices have been proposed for preparing sterile medical liquids at the place of use.

Document EP 0,622,087 describes a process for the on-line preparation of a sterile, pyrogen free liquid which is obtained by filtering a dialysis liquid produced by a standard dialysis machine.

Document GB 2,034,584 describes a process for preparing a sterile liquid whose sterility is obtained by heating the liquid to a determined sterilization temperature for a determined time. A device for carrying out this process, which is designed to fill bags with the sterile liquid, comprises:

- heating means for raising the temperature of a liquid immediately upstream of a sterilization unit consisting of a portion of heat-insulated circuit;

- a circuit connected to the sterilization unit, which has a first end connected to a source of liquid to be sterilized and a second end connected to a connector which has a first outlet for delivering a sterile liquid;

- a discharge pipe connected to a second outlet of the connector, and

- pumping means for circulating the liquid in the main circuit.

This device also comprises means for degassing by heating the liquid to be sterilized upstream of the heating means and of the sterilization unit in order to avoid the entrainment of bubbles by the liquid during the sterilization treatment.

Although that document presents the prior degassing as a satisfactory solution to the problem posed by the presence of bubbles in a liquid subjected to a sterilization treatment, it is doubted that, without other precautions, a liquid brought to a high temperature would not entrain bubbles simply because it has been degassed beforehand.

Moreover, that document avoids two questions which, according to the invention, need to be answered when the sterilization of a liquid is undertaken. The first question relates to what is meant by the term "sterilization" and the second question relates to the microbiological quality of the device used to carry out the sterilization.

It should be recalled that the term "sterility" defines a microbiological quality of the object said to be "sterile" and

that, according to standard EN 556 and also according to the US and European Pharmacopoeias, in order for a device or a liquid to be labeled as sterile, it is necessary for the theoretical probability of the presence of a viable microorganism in this device or this liquid to be less than or equal to 10^{-6}.

However, checking this 10^{-6} level of presence by examining the finished product is impossible on two counts, both because the sampling required for this check according to the Poisson probability distribution is unachievable, and because, in practical terms, the manipulations required to check the samples entail a probability of contamination which is such that, even if the sampling could be achieved, the results of the check would be erroneous.

One aim of the invention is to produce a sterilization process and a device for carrying out this process which ensure the sterility of the liquid prepared by the device according to the process.

In order to achieve this aim, a device is provided, in accordance with the invention, comprising:

- main adjustable heating means for raising the temperature of a liquid inside a heating chamber,
- a main circuit comprising:
  - a first pipe, one end of which can be connected to a source of liquid to be sterilized, and another end of which is connected to an inlet of the heating chamber, and
  - a second pipe, one end of which is connected to an outlet of the heating chamber, and another end of which is

connected to a connector which has a first outlet for delivering a sterile liquid,

- first pumping means for circulating the liquid in the main circuit,

characterized in that it comprises:

- means for validating a sterilization treatment applied to the liquid, comprising calculation means for calculating a parameter representing the sterilizing value (F0) for the treatment from the value for at least one operating parameter of the device (Q, Tin, THin, Tout, THout), and comparison means for comparing the calculated value of the parameter representing the sterilizing value (F0) to a first threshold value F0min1 corresponding to the sterility of the liquid.

For example, the calculation means are provided to calculate the parameter representing the sterilizing value (F0) for the treatment applied to the liquid from a mathematical model of the temperature distribution in the heating chamber, the temperature (Tin, Tout) of the liquid entering or leaving the heating chamber, the temperature of the heating liquid (THin) and the flow rate of the liquid (Q) in the heating chamber.

According to one characteristic of the invention, the device also comprises control means for controlling the pumping means and/or the heating means such that the calculated value of the parameter representing the sterilizing value (F0) is greater than the first threshold value F0min1.

According to another characteristic of the invention, the device also comprises means for preventing the formation of bubbles in the liquid during the sterilization of the liquid, these means comprising first means, such as a valve with adjustable opening, for adjusting the pressure of the liquid to a pressure value above the vaporization pressure of the liquid, irrespective of the temperature of the liquid, the first means for adjusting the liquid pressure being provided on the second pipe of the main circuit.

According to yet another characteristic of the invention, the device also comprises means for sterilizing the second pipe and the connector comprising:

- means for validating a sterilization treatment applied to the second pipe and to the connector, and
- means for preventing the formation of bubbles in the liquid during the sterilization of the second pipe and of the connector.

A subject of the invention is also a process consisting in:

- heating the liquid in a heating chamber to a temperature and for a period which are suitable for sterilizing the liquid;
- validating the sterilization treatment applied to the liquid by calculating a parameter representing the sterilizing value (F0) for the treatment from the value of at least one operating parameter for the device (Q, Tin, THin, Tout, THout), and by comparing the calculated value of the parameter

representing the sterilizing value (F0) to a first threshold value F0min1 corresponding to the sterility of the liquid.

Other characteristics and advantages of the invention will become apparent on reading the description which follows. Reference will be made to the attached drawings, in which:

Figure 1 represents the scheme of a first embodiment of a device according to the invention;

Figure 2 represents the scheme of a second embodiment of a device according to the invention;

Figure 3 is a view in perspective of a first embodiment of a heat exchanger according to the invention;

Figure 4 is a view in perspective of a second embodiment of a heat exchanger according to the invention.

The device for preparing and dispensing a sterile liquid, represented in Figure 1, essentially comprises main heating means 80 with a heating chamber 511 for the liquid, and a main circuit with a first pipe 1 connected to an inlet of the heating chamber 511 and a second pipe 2 connected to an outlet of the heating chamber 511.

The main heating means 80 comprise a reservoir 81 for a heating liquid (for example oil or ethylene glycol) connected via a heating liquid recirculation pipe 83 to a tubular sleeve 512 which surrounds the chamber 511 for heating the liquid to be sterilized. The heating chamber 511 and the sleeve 512 form a first heat exchanger 51. The main heating means 80 also comprise an adjustable heating member 84 for heating the heating liquid, as well as a pump 42 for permanently circulating the heating liquid in the exchanger 51.

The first pipe 1 has two inlets respectively controlled by means of two valves 20, 21: a first inlet is connected to a water source (valve 20) and the second inlet is connected to a source of medical liquid (valve 21). The following members are provided on the first pipe 1, in order, starting from the valves 20, 21: a conductivity meter 85 for measuring the conductivity of the liquid in the circuit and for checking whether the liquid is water or a solution; a filter 86; a degassing chamber 87 fitted with a level detector 88; a flow meter 74; a first pump 40; first additional heating means 501 and a valve 23. A purge pipe 3, which is fitted with a valve 22 and a non-return valve 89, connects a high point of the degassing chamber 87 to the drain. A branch pipe 4 fitted with a pump 41 is connected to the purge pipe 3 so as to short-circuit the valve 22. During functioning, each time the level detector 88 detects no more liquid, then either the valve 22 is opened for a determined period if the pressure of the liquid in the circuit upstream of the first pump 40 is above atmospheric pressure, or the pump 41 is switched on for a determined period, if the pressure of the liquid in the circuit upstream of the pump 40 is below atmospheric pressure.

The second pipe 2 connects the outlet of the heating chamber 511 to an outlet of the main circuit, which consists of a special sterilizable connector 90, with one inlet and two outlets. A connector of this type is described, for example, in patent No WO 96/05883. The following members are provided on the second pipe 2, in order, starting from the exchanger 51: first additional cooling means 502, which are advantageously combined with the first additional heating

means 501 to form a second heat exchanger 50; main cooling means comprising a tubular sleeve 521 surrounding the pipe 2 over a part 522 of its length to form a third heat exchanger 52, the sleeve 521 having an inlet connected to a cold water source via a feed pipe 5 on which is provided a pump 43, and an outlet connected to the drain via a discharge pipe 6 on which are provided, in order, starting from the exchanger 52: a valve 25 and a non-return valve 91; a first means of liquid pressure adjustment consisting of a valve 36 with adjustable opening; two valves 26, 27 which are in duplicate for safety reasons; and the sterilizable connector 90, which has an inlet connected to the end of the pipe 2, a first outlet (not shown) for connecting the device to a container or to a patient and a second outlet connected to one end of a first discharge pipe 7, the other end of which is connected to the drain.

As will be explained later in detail, the first discharge pipe 7 is used during the sterilization of the second pipe 2 and of the connector 2, and during the drainage of a patient's peritoneal cavity, when the device according to the invention is used for treating a patient by peritoneal dialysis. The following members are provided on the first discharge pipe 7, in order, starting from the connector 90: two valves 28, 29 which are in duplicate for safety reasons; a second additional cooling means 531; a second means of liquid pressure adjustment consisting of a valve 37 with adjustable opening, which can be by-passed by means of a branch pipe 8, fitted with a valve 30; a non-return valve 92; a second flow meter 75; a blood detector 95; a valve 31. A branch pipe 9 fitted with a valve 32 and a second pump 44 is connected to the

discharge pipe 7 so as to short-circuit the valve 31. As will be explained later in detail, the second pump 44 is used for draining the patient's peritoneal cavity. This second pump can also be used at the start of a step of filling a container or the peritoneal cavity of a patient subjected to a peritoneal dialysis treatment.

A second discharge pipe 10 has one end connected to the second pipe 2 of the main circuit, immediately downstream of the adjustable valve 36, and its other end is connected to the drain. This pipe 10 is provided, in order, starting from the second pipe 2, with a first valve 33, a second valve 34 and a non-return valve 93. As is described in detail later, this discharge pipe 10 is used during a peritoneal dialysis treatment, outside of the steps for filling the patient's peritoneal cavity.

The first and the second discharge pipes 7, 10 are connected via a connecting pipe 11, one end of which is connected to the pipe 7, between the valve 29 and the second additional cooling means 531, and the other end of which is connected to the pipe 10, between the valves 33 and 34. A valve 35 is provided on this connecting pipe 11.

The device for preparing and dispensing a sterile liquid according to the invention also comprises a third pipe 12 mounted in parallel to the first pipe 1, between a first point located downstream of the first pump 40 and a second point located upstream of the first exchanger 51. This third pipe 12 is provided, in order, starting from the pump 40, with a second additional heating means 532 and a valve 24. Advantageously, the second additional heating means 532 is

combined with the second additional cooling means 531 to form a fourth heat exchanger 53.

In accordance with the invention, the third pipe 12 and its accessories, along with the adjustable valve 37 provided on the first discharge pipe 7, form a part of means for sterilizing the device (second pipe 2 and connector 90).

The device represented in Figure 1 also includes a plurality of pressure and temperature measuring means provided at various points on the main circuit (pipes 1 and 2), on the first discharge pipe 7 and on the main heating means 80. In particular, a pressure sensor is connected to the following pipes, at the following points:

- on the second pipe 2, between the third exchanger 52 and the first adjustable valve 36 (reference number 70);
- on the second pipe 2, immediately upstream of the connector 90 (reference number 71);
- on the first discharge pipe 7, between the fourth exchanger 53 and the second adjustable valve 37 (reference number 72).

A temperature sensor is connected to the following pipes, at the following points:

- on the first pipe 1, immediately downstream of the first pump 40 (reference number 60);
- at the inlet and at the outlet of the heating chamber 511 of the main heating means 80 (reference numbers 63, 64);
- on the pipe 83 for recirculating the heating liquid, at the outlet of the reservoir 81 (reference number 61) and at the outlet of the sleeve 512 (reference number 62);
- on the second pipe 2, between the third exchanger 52 and the first adjustable valve 36 (reference number 65);

- on the second pipe 2, at the junction between this pipe and the second discharge pipe 10 (reference number 66);
- on the first discharge pipe 7, at the inlet of the fourth exchanger 53 (reference number 67);
- on the first discharge pipe 7, downstream of the second adjustable valve 37 (reference number 68).

Manufacturers of suitable components for the device of figure 1, as well as the reference of such components are indicated in the following table.

COMPONENT	FIGURE 1 REFERENCE N°	MANUFACTURER	MANUFACTURER REFERENCE
Blood leak detector	95	HOSPAL DASCO	6957989
Degassing chamber	87	HOSPAL DASCO	6965925
Conductivity meter	85	HOSPAL DASCO	6945109 6962195
Gear pump	43	HYDROFLUID	prototype HOSPAL RD
Peristaltic pump	41	ASF	6959100
Gear pump	40, 44	THUTILL	B9049PYWQS
Filter	86	HOSPAL DASCO	6958821
Flow meter	74, 75	HOSPAL DASCO	6955959
Heat exchanger	50, 51, 52, 53	PARKER FLUID CONNECTOR	type DHTC SS4
Level detector	88	HOSPAL DASCO	6957054
Main heating means	42, 80, 81, 84	BIOBLOCK	type HUBERT (G85111)
Recirculation pipe	83	PROLABO	06521000
Non-return valve	89, 91, 92, 93	HOSPAL DASCO	6950737
Sterilizable connector	90	CAMBRIDGE CONSULTANTS	prototype
Valve with adjustable opening	36, 37	NUPRO (SWAGELOK)	type RL3 (SS-3K-RL3-VI
Pressure sensor	70, 71, 72	KELLER	PA-10-8838
Solenoid valve	20, 21, 22, 25, 31, 32	SIRAI	D111S15Z612A
Solenoid valve	23, 24, 26, 27, 28, 29, 30, 33, 34 ,35	BÜRKERT	type 255 (35003999)
Stainless pipe	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12	FAURE AUTOMATISME	36403031
Temperature sensor	60, 61, 62, 63, 64, 65, 66, 67, 68	FAURE AUTOMATISME	TC2EJ20M3AJR1

The device according to the invention also includes a control unit (not shown). This unit receives the data measured by the pressure sensors 70 to 72, by the temperature sensors 60 to 68 and by the flow meters 74 and 75. From these data, from the set value for the operating parameters communicated by an operator (in particular, optionally, the flow rate of the liquid) and from a control and checking program stored in a memory of the control unit, this unit controls and checks the functioning of the device. In particular, in accordance with the invention, the control unit checks and validates the sterilization treatment applied to the liquid, on the one hand, and to the device, on the other hand.

In accordance with the invention, in order to ensure that the liquid leaving the main heating means 80 is sterile at all times, it is first necessary to define a parameter representing the sterilizing value for the treatment carried out, which can be calculated, for example, from an algorithm modeling the temperature distribution inside the exchanger 51 for the main heating means 80, and from the value of at least one of the parameters liable to influence the sterilization treatment, namely the flow rate Q of the liquid to be sterilized in the exchanger 51, the temperature (Tin) of the liquid to be sterilized entering the exchanger 51 and the temperature (THin) of the heating liquid entering the exchanger 51. Since the temperatures at the outlet of the exchanger 51 (temperature of the sterilized liquid and temperature of the heating liquid) are linked to the temperatures at the inlet of the exchanger 51, it also possible to take into account in the calculations the

temperature (Tout) of the sterilized liquid leaving the exchanger 51 and/or the temperature (THout) of the heating liquid leaving the exchanger 51.

When the parameter representing the sterilizing value for the treatment is defined, a set value for this parameter is then chosen which is both high enough to correspond to an effective sterilization of the liquid, and as low as possible in order to prevent or limit the degradation of the liquid to be sterilized when this liquid is heat-sensitive (as in the case of solutions for peritoneal dialysis which contain glucose).

During functioning, the control unit is programmed to calculate, at regular intervals, the value of the parameter representing the sterilizing value for the treatment, from the algorithm of temperature distribution in the exchanger 51, and the temperature and flow rate data measured by the corresponding sensors. Each time that a new value for the parameter is calculated, the control unit checks that this calculated value is higher than the set value and it validates the sterilization of liquid.

This checking process, which allows validation of the effective sterilization of the liquid as resulting from the correct use of the device according to the invention, can be passive. The reason for this is that, given that the sterile state is a crucial characteristic of a medical liquid which needs to be injected, it is possible to envisage a standard operating mode for the sterilization device in which the choice of the flow rate for the liquid to be sterilized is limited to a restricted number of different predetermined

values (for example three) and in which all of the other operating parameters for the device are preset as a function of the predetermined flow rates, such that the functioning of the device is simplified as much as possible. In this case, the checking process described above is used merely to validate the sterilization.

Naturally, it is also possible to envisage an operating mode for the device in which the choice of flow rate of liquid to be sterilized is free within a range of determined values. In this case, the control unit can be used to calculate, from the chosen flow rate and from the set value for the parameter representing the sterilizing value, the other operating parameters for the device, in particular the temperature of the heating liquid. During functioning, the control unit regularly adjusts the flow rate of the first pump 40 and/or the temperature of the heating liquid, such that the calculated value of the parameter is always greater than the set value.

In one embodiment of the invention, the parameter denoted in the literature as F0 (expressed in minutes) is used as parameter representing the sterilizing value for the sterilization process. It is recalled that F0 is the sum F_T^z of the cumulative sterilizing effects during a sterilization treatment (this sum being called "sterilizing value F_T^z") when the reference temperature T is equal to 250°F (121.1°C) and the thermal inactivation value Z is equal to 18°F (10°C). As a reminder, the thermal inactivation value Z is the temperature increase which multiplies by ten the rate of destruction of a

specific microorganism. Z = 10°C corresponds to a theoretical microorganism which is slightly more resistant than the microorganism reputed to be more heat-resistant than any other spore-forming microorganism, *Bacillus stearothermophilus*. The canonical formula of F0 is as follows:

$$F0=\int_0^t 10^{\left[\frac{T-121}{10}\right]} dt$$

This formula cannot be applied directly to the checking of a sterilization treatment in which the liquid to be sterilized is permanently flowing and in which the heating means used to raise the temperature of the liquid to be sterilized do not bring this liquid to the same temperature at all points in the heating chamber.

In accordance with the invention, when the heating means are arranged to heat the liquid to be sterilized along a portion of the pipe in which the liquid is circulating, the following formula can be used to calculate F0:

$$F0=\int_0^L \frac{S}{Q} \times 10^{\left[\frac{T(y)-121}{10}\right]} dy$$

in which

L = length of the portion of pipe (heating chamber 511) via which the liquid to be sterilized is heated by the heating means 80;

S = internal cross section of the heating chamber 511;

Q = flow rate of the liquid to be sterilized in the heating chamber 511;

T(y) = equation of the temperature distribution of the liquid as a function of the distance from the inlet of the heating chamber 511.

The equation T(y) depends on the structure of the exchanger 51 for the main heating means 80 and on its operating mode. For example, reference will be made to Figure 3 which represents a first embodiment of an exchanger which is adapted to the device of the invention. This exchanger consists of two concentric pipes, the outer pipe forming a sleeve 512 around the inner pipe, which constitutes the heating chamber 511 mentioned above.

During functioning, the liquid to be sterilized and the heating liquid (ethylene glycol) from the reservoir 81 are circulated in counter-flow, in the inner pipe (heating chamber 511) and in the outer pipe (sleeve 512). The inside diameter of the heating chamber 511 is chosen such that, in the range of flow rates which includes the flow rates for operating the sterilization device (for example, 100 to 400 ml/min.), the flow of the liquid to be sterilized is always turbulent.

For an exchanger with an inner pipe made of stainless steel and an outer pipe made of copper and having the following dimensions:

Length (cm)	222
Inner pipe volume (ml)	26
Outer pipe volume (ml)	105
Cross section of the inner pipe (cm^2)	0.117
Area of the annular space between the inner and outer pipes (cm^2)	0.502
Internal perimeter of the inner pipe (cm)	1.213
External perimeter of the inner pipe (cm)	1.995
Internal exchange area of the inner pipe (cm^2)	269
External exchange area of the inner pipe (cm^2)	443

the equation T(x) can be written in the following way:

$$T(y)=Tin+(THin-Tin)\times\frac{r\times[e^{-ny}-e^{-nL}]}{1-r\times e^{-nL}}$$

in which:

Tin = temperature of the liquid to be sterilized entering the heating chamber 511 (such as measured by the sensor 63).

THin = temperature of the heating liquid entering the sleeve 512 (such as measured by the sensor 61).

$$r=6\times10^{-5}\times Q^2-0{,}0577\,Q+19{,}084$$

$$n = -\frac{1}{L} \ln\left[\frac{301415 - 958{,}18Q + Q^2}{292{,}6 + 65{,}72Q - 0{,}200453Q^3 + 0{,}00020948}\right]$$

Q = flow rate of the liquid in the heating chamber 511.

As emerges from this example, it is possible to calculate the sterilizing value F0 at any moment, from a measurement of the temperature Tin of the liquid to be sterilized entering the exchanger 51, a measurement of the temperature THin of the heating liquid entering the exchanger 51, a measurement of the flow rate Q of liquid to be sterilized and an equation modeling the temperature distribution inside the exchanger 51.

Throughout all the operating phases of the device according to the invention in which the device is programmed to produce a sterile liquid (water or medical liquid), the control unit validates the sterilization treatment carried out by checking that the calculated sterilizing value F0 is always greater than a first threshold value F0min1 corresponding to the sterility of the liquid.

In accordance with the invention, during a preliminary phase of operating the device, the main circuit of the device has to be sterilized, from the exchanger 51 up to and including the connector 90, i.e. beyond the connector 90, for example up to the level of the temperature sensor 67 connected to the first sterilization pipe 7. The sterilization of the main circuit can be considered as effective when all of the

points in the main circuit downstream of the exchanger 51 have been brought, by means of the sterile liquid, to a minimum temperature T2 for a minimum period t2, which corresponds to a second set sterilizing value F0min2, such that:

$$F0min2 = t2 \times 10^{\left[\frac{T2-121}{10}\right]}$$

Validation of the sterilization of the main circuit can be made simply by the control unit by checking that, during an uninterrupted interval at least equal to t2, the temperature of the liquid measured by the temperature sensor 67 has constantly been above T2.

Since the sterilization of the device is to be carried out with sterile water, during the initial phase of sterilizing the device, the control unit must validate both the sterilization of the liquid and sterilization of the main circuit. In other words, the control unit must check both that the sterilizing value for the sterilization treatment applied to the liquid is greater than F0min1 and that the sterilizing value for the sterilization treatment applied to the circuit is greater than F0min2.

When the device is used to administer an automated peritoneal dialysis treatment, the functioning of the device essentially comprises the following four phases:

The first phase corresponds to the initial sterilization of the device.

The second phase corresponds to a standby state in which the device is kept sterile and produces sterile water at a low

flow rate. This second phase comes immediately after the initial sterilization of the device or between two active phases of functioning of the device, the filling of the patient's peritoneal cavity and the draining of this cavity after the liquid has dwelled therein for a determined period.

The third phase corresponds to the continuous production of the sterile solution for filling the patient's peritoneal cavity.

The fourth phase corresponds to the draining of the patient's peritoneal cavity while the device is kept sterile and produces sterile water at a low flow rate.

First phase: initial sterilization of the circuit.

In order to economize the liquid for medical use, the circuit is preferably sterilized with water (valve 20 open, valve 21 closed). During this first phase, which includes several steps, valve 23 is closed and valve 24 is open, such that the water made to circulate by the first pump 40 circulates in the third pipe 12. Moreover, the first adjustable valve 36 is fully open and the second adjustable valve 37 is only partially open, such that pressure in the circuit upstream of the valve is always greater than the pressure at which the water would begin to boil (if the water began to boil, it would not be possible to validate the sterilization of the circuit, since it would not be possible to certify that every point of the circuit has come into contact with water at a minimum temperature for a minimum uninterrupted period of time). The pumps 43 and 44 are not switched on.

In a first step of this first phase, the valves 26, 27, 28, 29, 30, 32, 34 are closed and the valves 33, 35, 31 are open, such that, downstream of the first adjustable valve 36, the water flows into a part of the second discharge pipe 10, into the connecting pipe 11 and then into the first discharge pipe 7.

In a second step of this first phase, the valves 26, 27, 28, 29 are open, such that the water then also flows into the end of the second pipe 2, through the connector 90, and then into the first discharge pipe 7, from its connection to the connector 90.

In a third step of the first phase, the valves 33, 35 are then closed, such that the water no longer circulates in the start of the second discharge pipe 10.

The duration of these three steps, as well as the flow rate of the water in the circuit, the degree of opening of the valve 37 and the intensity of the heating supplied by the main heating means 80 are either adjusted to preprogrammed values or are adjusted as a function of each other such that the sterilizing value for the sterilization treatment applied to the water and to the circuit is greater than the first and the second set value F0min1, F0min2. The control unit also checks that, given the actual operating conditions of the device, as measured by the various sensors, the effective sterilizing value is greater than F0min1 and than F0min2.

For example, during this first phase, the flow rate of water made to circulate by the pump 40 is adjusted to 250 ml/min., the pressure in the circuit upstream of the valve 37 is adjusted to seven bar and the temperature of

ethylene glycol entering the exchanger 51 is adjusted to 165°C (the pressure referred to throughout this document is the absolute pressure). The temperature of the water leaving the exchanger 51 is then at least equal to 153°C and the temperature upstream of the fourth exchanger 53, as measured by the sensor 67, is at least equal to 131°C. The duration of the various steps is chosen such that the sterilizing value of the sterilization treatment applied to the liquid is greater than 30 min. and the sterilizing value of the sterilization treatment applied to the circuit is greater than 30 min.

Second phase: placing the device on standby.

The main aim of this phase is to provide sterile water at a temperature of 37°C and at atmospheric pressure at the connector 90.

In a first step of this second phase, the valve 23 is open, such that the water made to circulate by the pump 40 flows both into the first pipe 1 and into the third pipe 12.

In a second step, the valve 24 is closed, such that the third pipe 12 is isolated. Moreover, the valve 25 for the main cooling means is open and the pump 43 is switched on. During this step, the water is cooled in the exchanger 52, which it leaves at about 37°C, while the first adjustable valve 36 is gradually closed and the second adjustable valve 37 is gradually opened, such that the water does not begin to boil at any time, irrespective of its temperature, and such that, when the adjustment of the valves 36, 37 is complete, the pressure upstream of the first adjustable valve 36 is about seven bar and the pressure upstream of the second adjustable valve 37 is about one bar (atmospheric pressure). The valve 30

mounted in parallel to the second adjustable valve 37 is closed.

In a third step, the valves 33, 34 are open, such that the water also flows in the second discharge pipe 10.

Lastly, in a fourth step, the valves 26, 27, 28, 29 are closed, such that the sterile water only flows in the second discharge pipe 10 and such that the water stands in the portion of circuit containing the connector 90. In this mode of operating the device, which is a standby mode, all of the sterile water is sent to the drain. For reasons of economy, the flow rate of the pump 40 is reduced to the minimum, i.e. down to a value (100 ml/min.) at which the flow of water in the heating chamber 511 remains turbulent. Preferably, the temperature of the liquid for heating the main heating means 80 is lowered accordingly. During this second phase, as in the phases which follow, the control unit checks at regular intervals that the sterilizing value F0 for the treatment applied to the water, as calculated from the measured values of the flow rate Q and of the temperatures (Tin, THin) at the exchanger 51 inlet, is always within a range of values which has the first set value F0min1 as a lower limit (for example between 30 min. and 40 min.).

Third phase: production of sterile medical liquid.

The aim of this third phase is to produce a sterile medical liquid and to infuse this liquid into the patient's peritoneal cavity. A first step consists in closing the valve 20 and opening the valve 21 which gives access to a source of medical liquid to be sterilized, such that the medical liquid replaces the water in the first pipe 1, in the second pipe 2

up to the first adjustable valve 36, and in the second discharge pipe 10.

The second step of the third phase consists in opening the valves 26, 27, 28, 29, 31 such that the sterile medical liquid replaces the water in the end of the second pipe 2, in the connector 90 and in the first discharge pipe 7. Next, the valves 33, 34 are closed, such that the liquid is now sent to the drain only via the first discharge pipe 7.

The third step consists in connecting the patient to be treated to the device by means of a flexible tube (not shown), one end of which is connected to the patient's catheter and another end of which is connected to the connector 90 of the device. During the preceding three steps, the flow rate of the medical liquid controlled by the pump 40 is adjusted to a set infusion flow rate suited to the patient. After the patient has been connected to the device, the flow rate of the liquid leaving the connector 90 (infusion flow rate) is process-linked to the comparison between the pressure measured by the pressure sensor 71 and a set pressure corresponding to a pressure which is acceptable for the patient. In order to vary the infusion flow rate, a first possibility consists in modifying the flow rate of the first pump 40, which may make it necessary to correspondingly modify the temperature of the heating liquid. In order not to have to vary the sterilization parameters (flow rate of the liquid, temperature of the heating liquid), another possibility consists in opening the valves 28, 29, 32, in closing the valve 31 and in setting the second pump 44 at the appropriate flow rate.

According to one variant of the invention, the filling of the patient's peritoneal cavity is not carried out at constant flow rate as soon as the patient is connected to the device, and the infusion at the nominal flow rate is preceded by a transient phase in which the flow rate is gradually increased until the nominal flow rate is reached. In order to be able to vary the infusion flow rate without having to modify the flow rate of the first pump 40 (i.e. the liquid sterilization parameters also), the first discharge pipe 7 and the second pump 44 are used to take a decreasing fraction of the liquid sterilized by the device from the connector 90 and to send it to the drain. To do this, before the patient is connected to the device, the valves 28, 29, 30, 32 are open, the valve 31 is closed and the second pump 44 is switched on at the same flow rate as the main pump 40. When the patient is connected to the device, the second pump 44 is controlled such that its flow rate decreases gradually until it becomes zero (pump 44 stopped).

This filling phase is complete either when a predetermined amount of liquid, calculated by means of the data supplied by the flow meters 74 and 75, has been infused, or when the pressure measured by the pressure sensor 71 reaches a predetermined pressure. In the latter case, the control unit calculates the total amount of liquid infused, by means of the data supplied by the flow meters 74, 75.

Fourth phase: draining the patient's peritoneal cavity.

This phase follows the standby phase described above, during which the device produces sterile water at a low flow rate in order to maintain the sterility of the device, this

sterile water being sent to the drain via the second discharge pipe 10. In therapeutic terms, the draining of the patient's peritoneal cavity is ordered when the liquid infused during the previous filling phase has dwelled in the peritoneal cavity for a predetermined period.

Compared with the standby phase, the valves 28, 29, 30, 32 are open and the pump 44 is switched on at a predetermined flow rate. The pump 44 is stopped when the amount of liquid drained is equal to the amount of liquid previously infused, increased by an amount of liquid corresponding to the weight which the patient should lose during each dwelling phase. In an alternative embodiment, the pump 44 is stopped when the pressure measured by the pressure sensor 71 reaches a determined low threshold.

At the end of this draining phase, the valve 20 is closed and the valve 21 is opened, such that the device again sterilizes the medical liquid.

Figure 2 represents a second embodiment of the device according to the invention. This device essentially comprises main heating means 80 with a chamber 511 for heating the liquid, and a main circuit with a first pipe 1 connected to an inlet of the heating chamber 511 and a second pipe 2 connected to an outlet of the heating chamber 511.

The main heating means 80 comprise a reservoir 81 containing a heating liquid, such as oil or ethylene glycol. The heating chamber 511, which is coil-shaped, is arranged in the reservoir 81 so as to be immersed in the heating liquid. An adjustable heating member 84 allows the temperature of the heating liquid to be raised. The heating means 80 also

comprise liquid homogenization means consisting of a pipe 83 connecting the lower part to the upper part of the reservoir 81, on which a pump 42 is provided.

The first pipe 1 has an inlet which can be connected either to a water source or to a source of medical liquid. The following members are connected to the first pipe 1, in order, starting from the inlet of the pipe 1: a flow meter 74; a first pump 40; a valve 23; a first and a second additional heating means 541, 551.

The second pipe 2 connects the outlet of the heating chamber 511 to an inlet of a sterilizable connector 90, which has a first outlet for dispensing the sterile liquid. The following members are connected to the second pipe 2, in order, starting from the main heating means 80: first additional cooling means 552, which are advantageously combined with the second additional heating means 551 to form a first heat exchanger 55; second additional cooling means 542, which are advantageously combined with the first additional heating means 541 to form a second heat exchanger 54; main cooling means 56; a valve 27; first pressure adjustment means 36, consisting of a valve tared to a first pressure threshold (five bar); and a valve 26.

The heat exchangers 54, 55 are preferably shaped like the exchanger represented in Figure 4, i.e. with the junction on a part of their length of the pipe 1 and of the pipe 2. The two portions of joined pipes are formed into twin helical coils, and both the inside and the outside of the cylinder thus formed are covered with a material which is a good heat conductor.

The main cooling means 56 comprise a reservoir 57 with an inlet connected to a cold water source via a pipe 5 and an outlet connected to the drain via a pipe 6 on which is provided a valve 25. A drain pipe 15 fitted with a valve 39 is connected to the pipe 5 so that the reservoir 57 drains under gravity when the supply of water to the pipe 5 is interrupted and the valves 25 and 39 are opened. The pipe 2 includes a coil-shaped portion 522, which is arranged in the reservoir 57 so as to be immersed in the cold water. The cooling means 56 are also fitted with liquid homogenization means consisting of a recirculation pipe 58 connecting the lower part to the upper part of the reservoir 57, on which is provided a pump 43. During functioning, the pump 43 is permanently running, and the temperature of the water leaving the cooling means 56, which is measured by a temperature sensor 65 connected to the pipe 2, is compared with a reference temperature: when the temperature of the water leaving the cooling means 56 exceeds the reference temperature, the valve 25 is opened until the temperature of the water leaving the cooling means has fallen below the reference temperature.

The sterilization device represented in Figure 2 also comprises a first discharge pipe 7 which is connected to a second outlet of the connector 90, as well as a second discharge pipe 10 which is connected to the second pipe 2 of the main circuit.

The first discharge pipe 7 is used for draining a patient's peritoneal cavity, when the device according to the invention is used for treating a patient by peritoneal dialysis; it is also used, partially, during the sterilization

of the second pipe 2 and of the connector 90. The following members are connected to the first discharge pipe 7, in order, starting from the connector 90: a first valve 28; a second valve 32; a second flow meter 75; a third valve 35; and a pump 44.

The second discharge pipe 10 has one end connected to the second pipe 2 of the main circuit, between the tared valve 36 and the valve 26, and its other end is connected to the drain. The second discharge pipe 10, which is provided with a first valve 33 and a second valve 34, is used during a peritoneal dialysis treatment, outside of the steps for infusing the patient.

The first and the second discharge pipes 7, 10 are connected via a connecting pipe 11, one end of which is connected to the pipe 7, between the valves 28 and 32, and the other end of which is connected to the pipe 10, between the valves 33 and 34. A valve 29 is provided on this connecting pipe 11.

The device represented in Figure 2 also comprises means used specifically for sterilizing the second pipe 2 of the main circuit and the connector 90, namely a third pipe 12 mounted in parallel to the first pipe 1, and a fourth pipe 13 mounted in parallel to the second discharge pipe 10.

One end of the third pipe 12 is connected to the first pipe 1, between the pump 40 and the valve 23, and its other end is connected to the first pipe 1, between the two heat exchangers 54, 55. A valve 24 and third additional heating means 532 are provided on this third pipe 12, in the direction of circulation of the liquid.

One end of the fourth pipe 13 is connected to the second discharge pipe 10, between the valves 33 and 34, and its other end is connected to the pipe 10 downstream of the valve 34. A third additional cooling means 531, a second pressure adjustment means consisting of a valve 37 tared to a second pressure threshold (three bar) and a valve 31 are connected to this fourth pipe 13, in the direction of circulation of the liquid. Advantageously, the third additional heating means 532 are combined with the third additional cooling means 531 to form a heat exchanger 53 shaped like the exchanger represented in Figure 4.

Like the device in Figure 1, the device represented in Figure 2 also includes a plurality of pressure and temperature measuring means provided at various points on the main circuit (pipes 1 and 2), on the first discharge pipe 7, on the main heating means 80 and on the main cooling means 56. In particular, a pressure sensor is connected to the following pipes, at the following points:

- on the first pipe 1, between the valve 23 and the second exchanger 54 (reference number 70);
- on the first discharge pipe 7, between the valves 32 and 35 (reference number 71).

A temperature sensor is connected to the following pipes, at the following points:

- on the first pipe 1, at the outlet of the heating chamber 511 for the main heating means 80 (reference number 64);
- on the pipe 83 for recirculating the heating liquid (reference number 62);

- on the pipe 58 for recirculating the cooling liquid (reference number 60);
- on the second pipe 2, between the main cooling means 56 and the valve 36 tared to a first pressure threshold (reference number 65).

The device represented in Figure 2 also includes a control and checking unit (not shown). This unit receives the data measured by the pressure sensors 70, 71, by the temperature sensors 60, 62, 64, 65 and by the flow meters 74 and 75. From these data, from operating parameters communicated by an operator, and from calculation algorithms and control programs stored in a memory, the control unit controls and checks the various operating phases of the device.

The functioning of this device is not fundamentally different from the functioning of the device represented in Figure 1.

During the sterilization phase of the pipe 2 and of the connector 90, the main cooling means 56 are not switched on: the pump 43 is stopped, the valves 25 and 39 are open, and the supply of water to the pipe 5 is interrupted so that the reservoir 57 is empty. The valves 24, 26, 27, 28, 29, 31 are open and the valves 23, 32, 33, 34, 35 are closed. When the circuit including the pipe 2 and of the connector 90 has been sterilized, the section of pipe 10 between its junction with pipe 2 and its junction with pipe 11 is sterilized in turn, by opening valve 33 and closing one of the valves 26, 28, 29. For example, the pressure in the main circuit between the pump 40 and the valve 36 tared to the first pressure value is five

bar, the pressure between the valve 36 and the valve 37 tared to the second pressure value is three bar and the pressure downstream of the valve 37 is one bar (atmospheric pressure). The temperature of the heating liquid is adjusted such that, with suitable heat exchanger designs, and at an appropriate flowrate, the temperature of the water in line 12 downstream of the third exchanger 53 is 110°C, the temperature of the water at the outlet of the heating chamber 511 is 150°C, the temperature of the water downstream of the first and second exchangers 54, 55 and upstream of the third exchanger 53 is 130°C, and the temperature of the water in line 13 downstream of the third exchanger 53 is 60°C. The period for which the second pipe 2 and the connector 90 are left in contact with sterile water at 130°C is sufficient to ensure their sterility, that is to say also that the sterilizing value F0 for the sterilization treatment applied to them is greater than the second threshold value F0min2.

During the standby phase in which the device is kept sterile, the valves 23, 27, 33, 34 are open and the valves 24, 26, 28, 29, 31, 32, 33, 35 are closed. The main cooling means 56 are switched on (pump 43 running, valve 39 closed, valve 25 intermittently open).

During the phase of infusing liquid, the valves 23, 26, 27, 28, 32 are open and all of the other valves are closed. The main cooling means 56 are switched on (pump 43 running, valve 25 intermittently open).

For example, during these last two phases, the pressure in the main circuit between the pump 40 and the valve 36 tared to the first pressure value is five bar and the pressure

downstream of the valve 36 is one bar (atmospheric pressure). The temperature of the heating liquid is adjusted such that, with suitable heat exchanger designs, the temperature of the water at the outlet of the heating chamber 511 is 150°C, the temperature of the water downstream of the first and second exchangers 54, 55 is 60°C, and the temperature of the water downstream of the main cooling means is 37°C. For liquid flow rates less than or equal to about 300 ml/min., the operating conditions which have just been mentioned make it possible to ensure that the water or the medical liquid produced by the device is sterile. In other words, the sterilizing value F0 for the sterilization treatment applied to the water or to the medical liquid is greater than the first threshold value F0min1.

The invention is not limited to the embodiments which have just been described and is capable of variation.

CLAIMS

1. Device for preparing a sterile liquid, comprising:

- main adjustable heating means (80) for raising the temperature of a liquid inside a heating chamber (511),
- a main circuit comprising:
  - a first pipe (1), one end of which can be connected to a source of liquid to be sterilized, and another end of which is connected to an inlet of the heating chamber (511), and
  - a second pipe (2), one end of which is connected to an outlet of the heating chamber (511), and another end of which is connected to a connector (90) which has a first outlet for delivering a sterile liquid,
- first pumping means (40) for circulating the liquid in the main circuit (1, 2),

characterized in that it comprises:

- means for validating a sterilization treatment applied to the liquid, comprising calculation means for calculating a parameter representing the sterilizing value (F0) for the sterilization treatment from the value for at least one operating parameter of the device (Q, Tin, THin, Tout, THout), and comparison means for comparing the calculated value of the parameter representing the sterilizing value (F0) to a first threshold value F0min1 corresponding to the sterility of the liquid.

2. Device according to Claim 1, characterized in that it also comprises control means for controlling the pumping means (40) and/or the heating means (80) such that the calculated value of the parameter representing the sterilizing value (F0) is greater than the first threshold value F0min1.

3. Device according to either of Claims 1 and 2, characterized in that the calculation means are provided to calculate the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the liquid from a mathematical model of the temperature distribution in the heating chamber (511), the temperature (Tin, Tout) of the liquid entering or leaving the heating chamber (511), the temperature of the heating liquid (THin) and the flow rate of the liquid (Q) in the heating chamber (511).

4. Device according to Claim 3, characterized in that the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the liquid is the sterilizing value F0, defined by:

$$F0 = \int_0^L \frac{S}{Q} \times 10^{\left[\frac{T(y)-121}{10}\right]} dy$$

where

- L is the length of the heating chamber (511);
- S is the cross section of the heating chamber (511);
- Q is the flow rate of the liquid in the heating chamber (511);

- T(y) is an equation of the temperature distribution in the heating chamber (511).

5. Device according to one of Claims 1 to 4, characterized in that it also comprises means (36, 37) for preventing the formation of bubbles in the liquid during the sterilization of the liquid.

6. Device according to Claim 5, characterized in that the means for preventing the formation of bubbles in the liquid during the production of sterile liquid comprise first means (36) for adjusting the pressure of the liquid to a pressure value above the vaporization pressure of the liquid, irrespective of the temperature of the liquid, the first means (36) for adjusting the liquid pressure being provided on the second pipe (2) of the main circuit.

7. Device according to one of Claims 1 to 6, characterized in that it also comprises a first discharge pipe (7) for connecting a second outlet of the connector (90) to the drain.

8. Device according to one of Claims 1 to 7, characterized in that it also comprises a second discharge pipe (10) connected to the second pipe (2) of the main circuit between the first pressure adjustment means (36) and the connector (90).

9. Device according to one of Claims 1 to 8, characterized in that it includes first additional liquid heating means (501; 541, 551) provided on the first pipe (1) of the main circuit.

10. Device according to one of Claims 1 to 9, characterized in that it includes main liquid cooling means (5, 6, 43, 521; 56) provided on the second pipe (2) of the main circuit upstream of the first pressure adjustment means (36).

11. Device according to one of Claims 1 to 10, characterized in that it includes additional liquid cooling means (502, 542, 552) provided on the second pipe (2) of the main circuit upstream of the main liquid cooling means (5, 6, 43, 521; 56).

12. Device according to one of Claims 1 to 11, characterized in that it also comprises means (12, 37, 532; 12, 13, 37, 532) for sterilizing the second pipe (2) and the connector (90) for delivering the sterile liquid.

13. Device according to Claim 12, characterized in that the means for sterilizing the second pipe (2) and the connector (90) comprise second additional liquid heating means (532) provided on a pipe (12) mounted in parallel to the first pipe (1) of the main circuit.

14. Device according to Claim 13, characterized in that the first additional liquid heating means provided on the first pipe (1) of the main circuit include two components (541, 551) and in that the upstream end of the branch pipe (12) is connected to the first pipe (1) between the two components (541, 551) of the first additional heating means.

15. Device according to one of Claims 12 to 14, characterized in that the means for sterilizing the second pipe (2) and the connector (90) comprise means (37) for preventing the formation of bubbles in the liquid during the sterilization of the second pipe (2) and of the connector (90).

16. Device according to Claim 15, characterized in that the means for preventing the formation of bubbles in the liquid during the sterilization of the second pipe (2) and of the connector (90) comprise second means (37) for adjusting the pressure of the liquid to at least a pressure value above the vaporization pressure of the liquid, irrespective of the temperature of the liquid, the liquid pressure adjustment means being provided on the first discharge pipe (7).

17. Device according to one of Claims 12 to 16, characterized in that the means for sterilizing the second pipe (2) and the connector (90) comprise means for validating a sterilization treatment applied to the second pipe (2) and to the connector (90).

18. Device according to Claim 17, characterized in that the validation means comprise:

- calculation means for calculating a parameter representing the sterilizing value (F0) for the sterilization treatment from a minimum value T of the temperature of the liquid, measured during a determined period of time t, at a point on the first discharge pipe (7), and

- means for comparing the calculated value of the parameter representing the sterilizing value (F0) to a second threshold value F0min2 corresponding to the sterility of the second pipe (2) and of the connector (90).

19. Device according to Claim 18, characterized in that it also comprises control means for controlling the pumping means (40) and/or the main heating means (80) such that the calculated value of the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the second pipe (2) and to the connector (90) is greater than the second threshold value F0min2.

20. Device according to Claim 18, characterized in that the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the second pipe (2) and to the connector (90) is the sterilizing value F0, defined by :

$$F0 = t \times 10^{\left[\frac{T-121}{10}\right]}$$

where

- T = minimum value of the temperature of the liquid
- t = period of time t during which the minimum value T of the temperature of the liquid is measured.

21. Device according to Claims 6 and 16, characterized in that the first and the second liquid pressure adjustment means consist of a first and a second valve (36, 37) with variable

opening and in that the control means are designed to control, at the end of a step of sterilizing the first pipe (2) and the connector (90), the gradual partial closure of the first valve (36) and the gradual complete opening of the second valve (37).

22. Device according to Claim 7, characterized in that it includes second pumping means (44) provided on the first discharge pipe (7, 9).

23. Device according to Claim 22, characterized in that, at an initial stage of an operating phase of the device, the control means are designed to control the first pumping means (40) so that the flow rate of the liquid in the main circuit (1, 2) is substantially constant and the second pumping means (44) so that the flow rate of liquid in the first discharge pipe (7) gradually decreases, such that the flow rate of liquid flowing via the first outlet of the connector (90) gradually increases.

24. Device according to one of the Claims 1 to 23, characterized in that the main adjustable heating means (80) for raising the temperature of a liquid inside the heating chamber (511), comprises:

- a container (512, 81) for containing a heating liquid in which the heating chamber (511) is immersed;
- means (84) for heating the heating liquid.

25. Device according to the Claim 24, characterized in that the main adjustable heating means (80) further comprises means (42, 58, 83) for maintaining the temperature of the heating liquid substantially constant along the heating chamber (511).

26. Device according to one of the Claims 24, 25, characterized in that the heating chamber is pipe (511) and the container for the heating liquid is pipe (512) which is concentric to the heating chamber.

27. Process for sterilizing and dispensing a liquid by means of a device including:

- main adjustable heating means (80) for raising the temperature of a liquid inside a heating chamber (511),
- a main circuit comprising:
  - a first pipe (1), one end of which can be connected to a source of liquid to be sterilized, and another end of which is connected to an inlet of the heating chamber (511), and
  - a second pipe (2), one end of which is connected to an outlet of the heating chamber (511), and another end of which is connected to a connector (90) which has a first outlet for delivering a sterile liquid,
- a discharge pipe (10) connected to a second outlet of the connector (90),

characterized in that it consists in:

- heating the liquid in the heating chamber (511) to a temperature and for a period which are suitable for sterilizing the liquid;
- validating the sterilization treatment applied to the liquid by calculating a parameter representing the sterilizing value (F0) for the sterilization treatment from the value of at least one operating parameter for the device (Q, Tin, THin, Tout, THout), and by comparing the calculated value of the parameter representing the sterilizing value (F0) to a first threshold value F0min1 corresponding to the sterility of the liquid.

28. Process according to Claim 27, characterized in that it also consists in controlling the pumping means (40) and/or the heating means (80) so that the calculated value of the parameter representing the sterilizing value (F0) is greater than the first threshold value F0min1.

29. Process according to either of Claims 27 and 28, characterized in that it consists in calculating the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the liquid from a mathematical model of the temperature distribution in the heating chamber (511), the temperature (Tin, Tout) of the liquid entering or leaving the heating chamber (511), the temperature of the heating liquid (THin) and the flow rate of the liquid (Q) in the heating chamber (511).

- heating the liquid in the heating chamber (511) to a temperature and for a period which are suitable for sterilizing the liquid;
- validating the sterilization treatment applied to the liquid by calculating a parameter representing the sterilizing value (F0) for the sterilization treatment from the value of at least one operating parameter for the device (Q, Tin, THin, Tout, THout), and by comparing the calculated value of the parameter representing the sterilizing value (F0) to a first threshold value F0min1 corresponding to the sterility of the liquid.

28. Process according to Claim 27, characterized in that it also consists in controlling the pumping means (40) and/or the heating means (80) so that the calculated value of the parameter representing the sterilizing value (F0) is greater than the first threshold value F0min1.

29. Process according to either of Claims 27 and 28, characterized in that it consists in calculating the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the liquid from a mathematical model of the temperature distribution in the heating chamber (511), the temperature (Tin, Tout) of the liquid entering or leaving the heating chamber (511), the temperature of the heating liquid (THin) and the flow rate of the liquid (Q) in the heating chamber (511).

30. Process according to Claim 29, characterized in that the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the liquid is the sterilizing value F0, defined by:

$$F0=\int_0^L \frac{S}{Q} \times 10^{\left[\frac{T(y)-121}{10}\right]} dy$$

where

- L is the length of the heating chamber (511);
- S is the cross section of the heating chamber (511);
- Q is the flow rate of the liquid in the heating chamber (511);
- T(y) is an equation of the temperature distribution in the heating chamber (511).

31. Process according to one of Claims 27 to 30, characterized in that it also consists in preventing the formation of bubbles in the liquid during the sterilization of the liquid.

32. Process according to Claim 31, characterized in that it consists in pressurizing a part of the main circuit (1, 2) connected to heating chamber (511) such that, irrespective of the temperature of the liquid, the pressure of the liquid is always greater than the vaporization pressure of the liquid.

33. Process according to one of Claims 27 to 32, characterized in that it also consists in sterilizing the second pipe (2) and the connector (90), by bringing the second pipe (2) and

the connector (90) in contact with a sterile liquid at a temperature and for a period which are suitable for sterilizing this pipe (2) and this connector (90).

34. Process according to Claim 33, characterized in that it also consists in preventing the formation of bubbles in the liquid during the sterilization of the second pipe (2) and of the connector (90).

35. Process according to Claim 34, characterized in that it consists in pressurizing at least the second pipe (2), the connector (90) and a part of the discharge pipe (7) such that, irrespective of the temperature of the liquid, the pressure of the liquid is always greater than the vaporization pressure of the liquid.

36. Process according to one of Claims 33 to 35, characterized in that it also consists in validating the sterilization treatment applied to the second pipe (2) and to the connector (90).

37. Process according to Claim 36, characterized in that it consists, in order to validate the sterilization treatment applied to the second pipe (2) and to the connector (90),

- in calculating a parameter representing the sterilizing value (F0) for the sterilization treatment from a minimum value T of the temperature of the liquid, measured during a determined period of time t, at a point on the first discharge pipe (7), and

- in comparing the calculated value of the parameter representing the sterilizing value (F0) to a second threshold value F0min2 corresponding to the sterility of the second pipe (2) and of the connector (90).

38. Process according to Claim 37, characterized in that it consists in controlling the pumping means (40) and/or the main heating means (80) so that the calculated value of the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the second pipe (2) and to the connector (90) is greater than the second threshold value F0min2.

39. Process according to Claim 38, characterized in that the parameter representing the sterilizing value (F0) for the sterilization treatment applied to the second pipe (2) and to the connector (90) is the sterilizing value F0, defined by:

$$F0 = t \times 10^{\left[\frac{T-121}{10}\right]}$$

where

- T = minimum value of the temperature of the liquid
- t = period of time during which the minimum value T of the temperature of the liquid is measured.

40. Process according to Claims 32 and 35, characterized in that it consists in pressurizing the part of the main circuit (1, 2) connected to the main heating means (80) by means of a

first valve (36) with variable opening, and in pressurizing at least the second pipe (2), the connector (90) and a part of the discharge pipe (7) by means of a second valve (36) with variable opening.

41. Process according to Claim 40, characterized in that it consists in controlling, at the end of a step of sterilizing the first pipe (2) and the connector (90), the gradual partial closure of the first valve (36) and the gradual complete opening of the second valve (37).

42. Process according to one of Claims 27 to 41, characterized in that it consists, at an initial stage of a phase of producing sterile liquid, in causing a flow of the liquid in the main circuit (1, 2) at a substantially constant flow rate, and in causing a flow of liquid in the discharge pipe (7) at a gradually decreasing flow rate, such that the flow rate of liquid available at the first outlet of the connector (90) gradually increases.

43. Process according to one of Claims 27 to 42, characterized in that the flow rate of the liquid to be sterilized is chosen so that the flow of the liquid is turbulent in the heating chamber (511).

ABSTRACT

A device for preparing a sterile liquid, comprises means for validating a sterilization treatment applied to the liquid, comprising calculation means for calculating a parameter representing the sterilizing value (F0) for the sterilization treatment from the value for at least one operating parameter of the device (Q, Tin, THin, Tout, THout), and comparison means for comparing the calculated value of the parameter representing the sterilizing value (F0) to a first threshold value F0min1 corresponding to the sterility of the liquid.

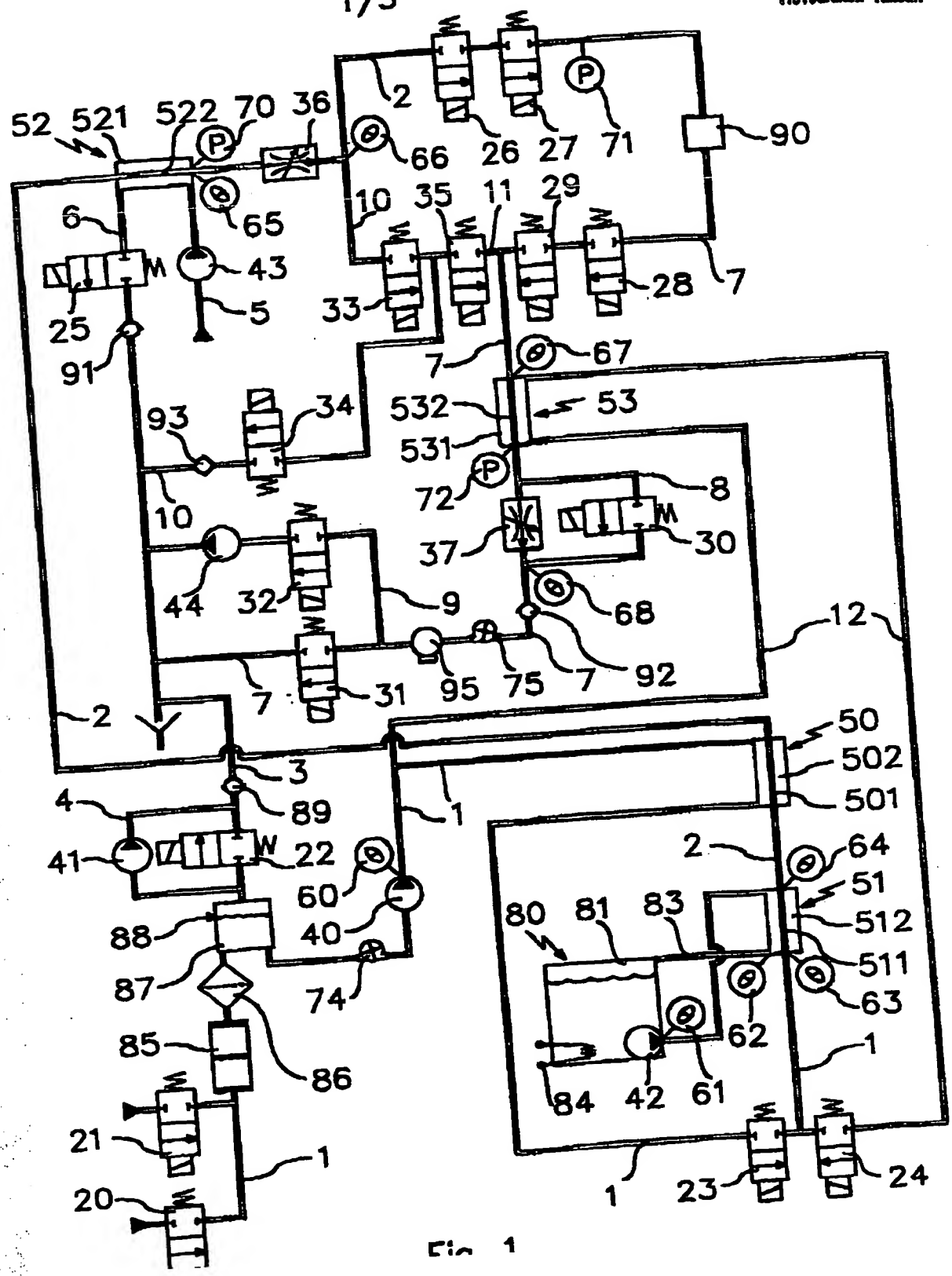


Fig. 1

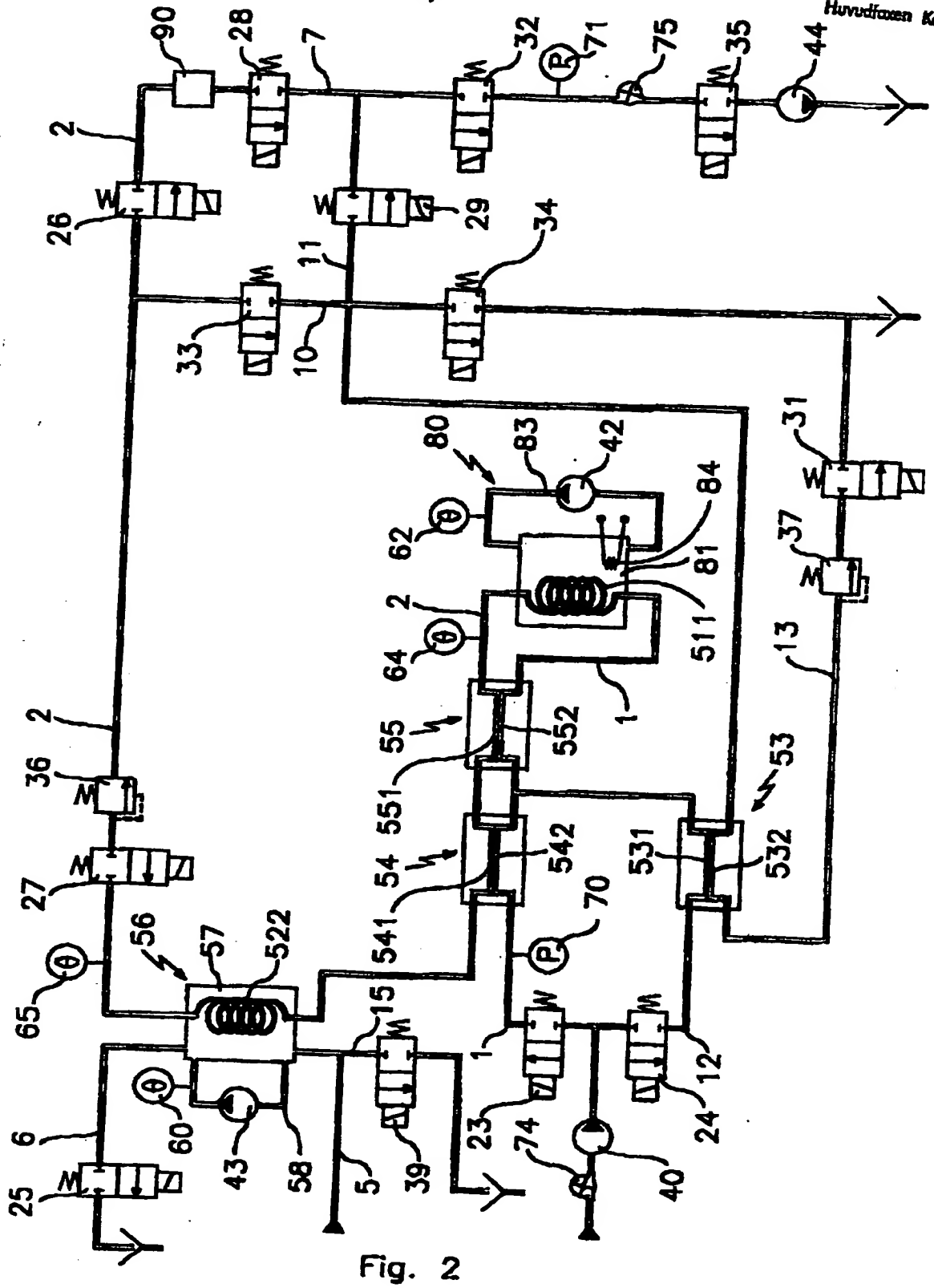

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Fig. 2

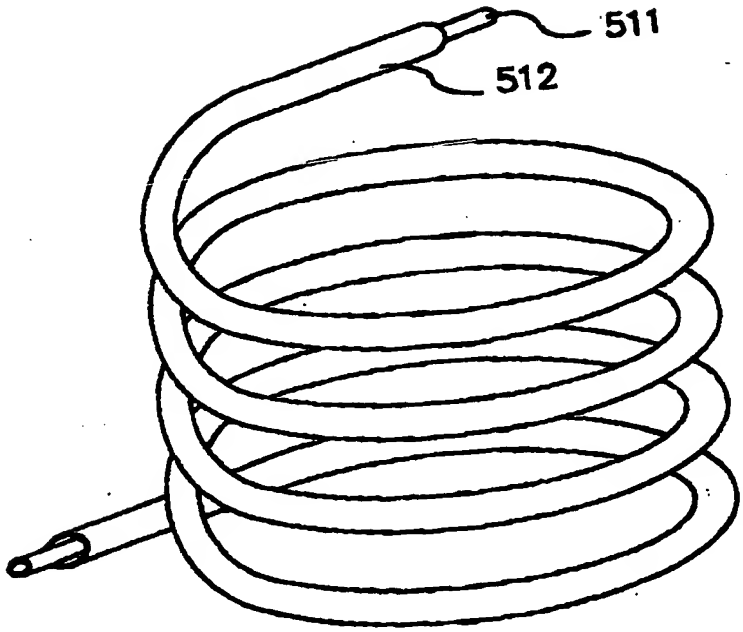

Fig. 3

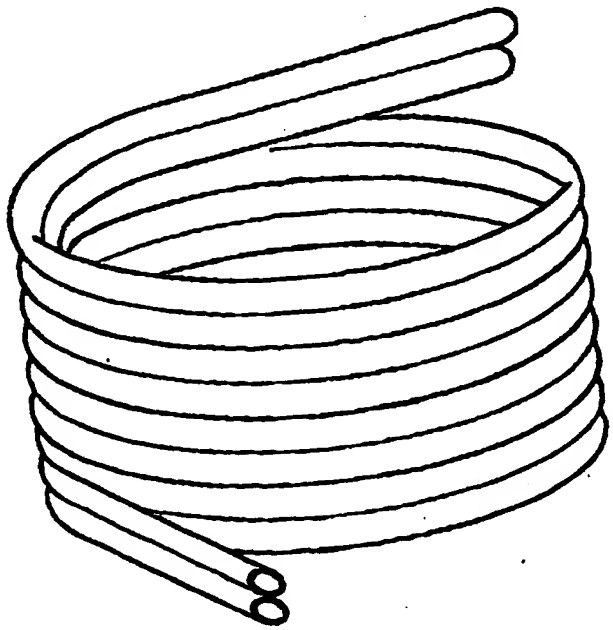

Fig. 4

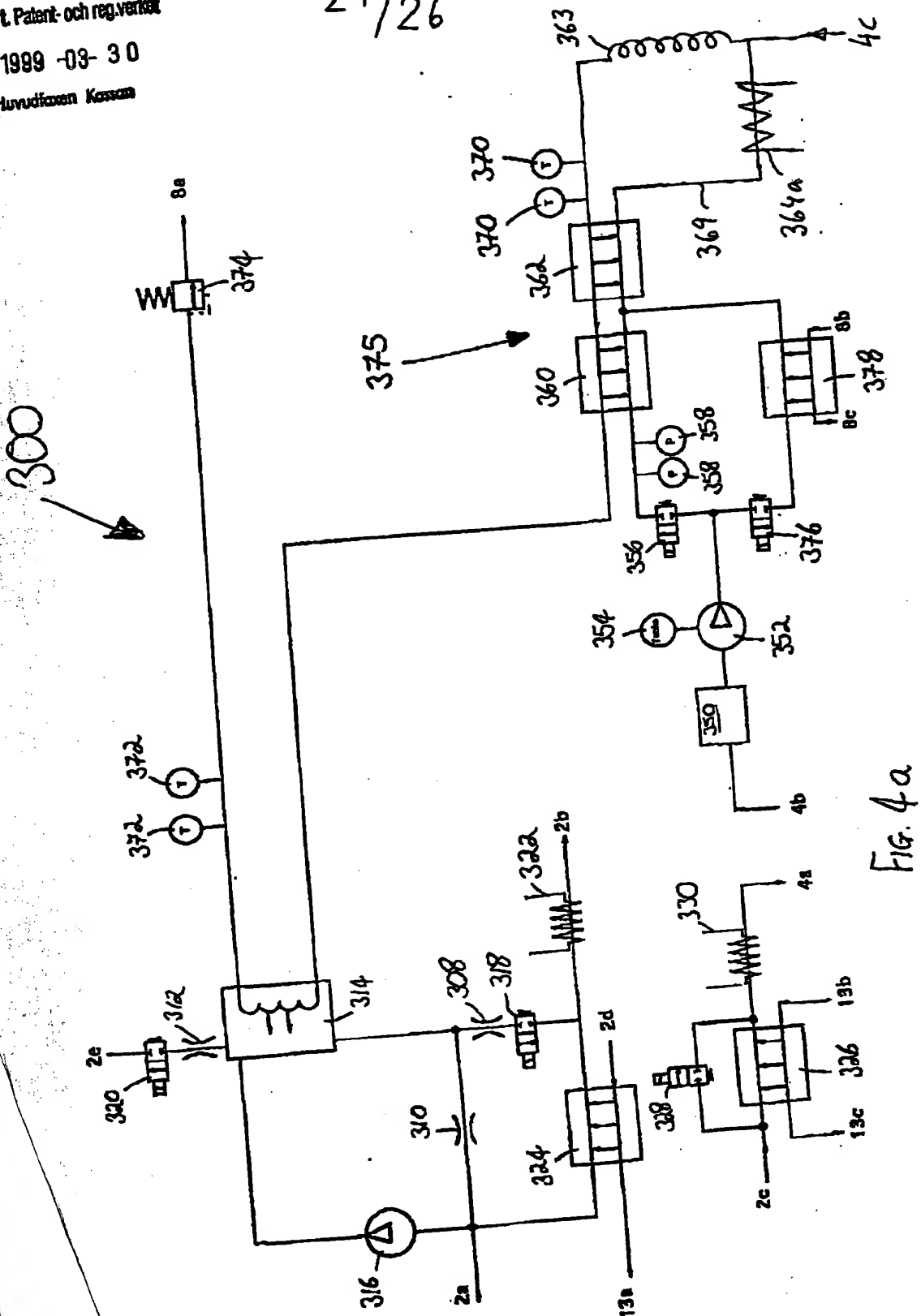

Fig. 4a

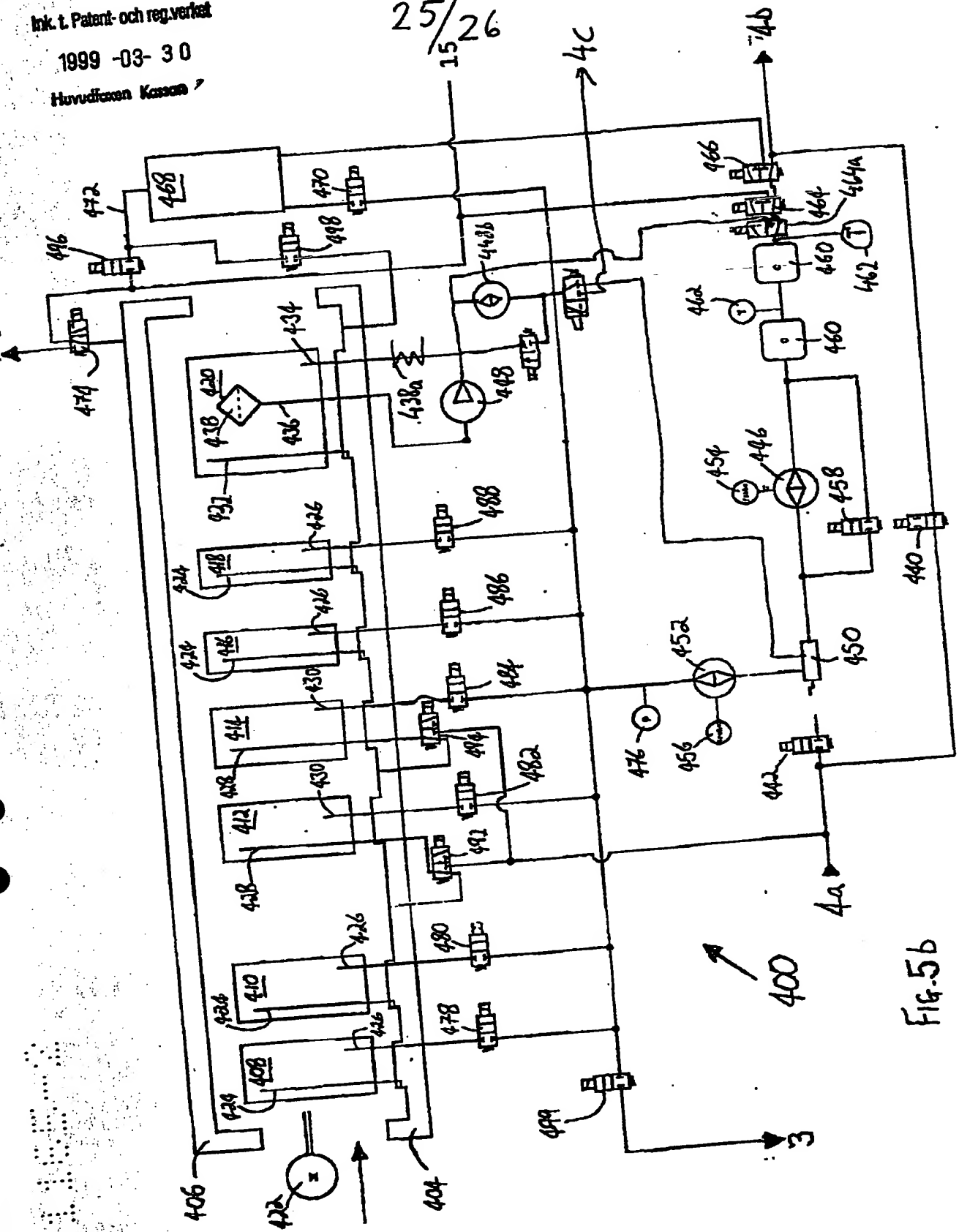

Fig. 5b

FIG. 23